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Vol. XXII, No. 1 JANUARY, 1933

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 81st ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN MADISON, WISCONSIN, AUGUST 28-SEPTEMBER 2, 1933, HOTEL LORAINE, HEADQUARTERS, EMERSON STANLEY, 602 CENTRAL BUILDING, MADISON, LOCAL SECRETARY.

The 1933 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Madison.

Entered as second-class Matter, January 23, 1917, at the Post Office at Easton, Pa., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in section 1103. Act of October 3, 1917; authorized July 10, 1918.

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ALLONAL . . . . *for pain and sleeplessness*

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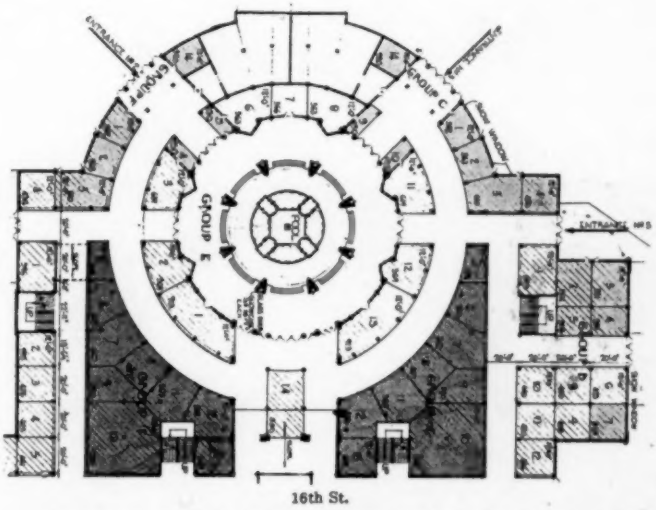
PHARMACY IN THE CENTURY OF PROGRESS.



Entering from 16th Street and turning into the circle to the right the Pharmacy Exhibit is reached, the units of which are Historical, Educational and Professional and include a number of divisional exhibits. In the immediate vicinity are exhibits of the Wellcome Museum, Pasteur Institute, etc. Fronting entrance No. 9 is the "Transparent Man," visualizing the human anatomy, and above the entrance the exhibits of the American Medical Association, American Dental Association, etc.

The Historical Rotunda tells the story of discoveries, and spaces are assigned to portraits or busts of famous pharmacists; the American Pharmacy Building will be featured. In order to interest the public it is suggested that a portion of Ebers Papyrus be reproduced, showing the World's oldest prescription.

ROBERT L. SWAIN.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXII JANUARY, 1933 No. 1

THE PRESIDENT-ELECT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The president-elect for 1933–1934, of the AMERICAN PHARMACEUTICAL ASSOCIATION, is a native of the State first to sign the Federal Constitution and named in honor of one of the early governors of Virginia; the state of his adoption is Maryland.

Robert Lee Swain, son of the late Rev. C. P. Swain, and Martha H. (née Messick) Swain, was born at Redden, Sussex County, Delaware, September 29, 1887, where he received his earlier education; later, the young man completed the course at Dover High School and thereafter entered the School of Pharmacy, University of Maryland, from which institution he graduated in 1900. Mr. Swain purchased a pharmacy in Sykesville, Md., which he conducted successfully until 1927, when other duties made it necessary for him to dispose of it. In 1922, he was elected Deputy Food and Drug Commissioner of Maryland, an office he still holds and the duties of which are being discharged in the interest of the State, the benefit of its citizens and reflect credit upon him.

Governor Ritchie, in 1920, appointed him member of the Maryland Board of Pharmacy and reappointed him in 1925, since which time he has served as its *Secretary-Treasurer*. He makes effective his belief in coöperation of the drug-trade activities, with pharmacy as fundamental, and the service of the public. Soon after graduation he became a member of the Maryland Pharmaceutical Association to which body he has rendered distinguished services, not the least of which is as editor of the *Maryland Pharmacist*—an outstanding publication, because the purposes of its establishment are the guide-posts; contact with state and national affairs are maintained, with a realization that the benefits are reciprocal and promote pharmacy as a Public Health service. He has an active part in State Association affairs, in coördinating its program and activities.

The president-elect became a member of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1909, and has been a regular attendant at its annual meetings, participating actively at its sessions and during the interim; he served as president

of the Baltimore Branch, A. PH. A., for two terms; in 1928 Mr. Swain was elected vice-chairman of the House of Delegates and, in 1929, chairman. He is chairman of the Committee on Pharmacy Corps in the U. S. Army. His vocational duties have contributed largely to his committee work, thus, through his suggestion the Conference of Law Enforcement Officials was established and has become an important part of the ASSOCIATION'S activities. He has been chairman since its establishment.

Likewise, his interest in educational affairs is evidenced and reflected in his reports and contributions to various programs. His reports are clearly stated, his addresses are forceful and worth while messages; all of them evidence thought, study and purpose.

Since the publication of a prior sketch in 1929,[1] the president-elect has completed the course in law of the School of Law, University of Maryland—earned his degree and the right to practice law.

Underwood & Underwood

The above shows the newly completed model of down-town Washington's transformation in the section where the Pharmacy Building is located. The model is to be shown at the Chicago World's Fair. The Memorial Bridge, Lincoln Memorial and Washington Monument are easily located. The Headquarters site is indicated by circle and cross.

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[1] November JOURNAL, 1929, page 1101.

EDITORIAL

E. G. EBERLE, EDITOR 10 West Chase Street, BALTIMORE, MD.

DEATH OF MR. COOLIDGE.

FEW Presidents have lived many years after the conclusion of their years of service in the highest office within the peoples' gift. The passing of Mr. Coolidge brings general expression of sympathy to one who modestly but largely contributed to the services rendered by the late President to the country. We are not called upon to place an estimate on the life of the deceased, but it is becoming to lament his death, and speak with due reverence of him as a distinguished and honored citizen who had gained the respect and affection of his countrymen to a degree that will remain his most enduring monument.

OUTSTANDING EVENTS OF PHARMACY IN 1933.

TWO outstanding events will mark Pharmacy in 1933. The American Pharmacy Building in Washington is well under way and there is hopeful assurance that it will be completed this year, marking an event of greatest importance for pharmacy.

The Pharmacy exhibit at the "Century of Progress"—Chicago World's Fair—presents an outstanding opportunity for acquainting the public with the part of Pharmacy in the advancement of civilization, medical progress and public health service. Pharmacy has been alloted liberal space in the fountain circle—on the ground floor of the Hall of Science, among the groups that are related to pharmacy, completing its story to be told by the exhibit and dramatized in a manner that will impress its significance on the visitors.

An interesting description has been given by Chairman H. C. Christensen which is drawn upon in the following. The space for the Pharmacy exhibit is irregular and in its designing these irregularities have been framed into a simple geometric plan. Interesting forms of light and color attract the visitors and center attention on the exhibit. There is an inviting atmosphere of openness and freedom. Plain walls turning inward from each side and spiral forms draw the visitor in and permit a natural circulation to the entire display, taking them to each point of interest and letting them out again without the feeling of having been led by rules or directions. No doorways, gates or railings impede their individual interests. (See page 1.)

The aim of the exhibit is to show professional progress—the drug store of a hundred years ago will be contrasted with a pharmacy of to-day. The history will be depicted in various divisions and the preparation of the U. S. Pharmacopœia and the National Formulary will be illustrated by the results of revision work. Apparatus of different periods and pharmaceutical literature will contribute to the story of pharmacy.

As an example of display "digitalis" has been mentioned, telling the story in a series of panels—its interesting history, plant life, botany and pharmacognosy, pharmacy and pharmacology. Other drugs will be illustrated in like manner, including the bibliography, and biographical sketches of those who contributed to

the development of the materia medica. The story told of animal and vegetable drugs will find related application in chemicals and other products from various sources, and the reasoning which guided earlier investigators will be compared with the researches of present day. The value of the famous discoveries of pharmacists will be brought to the attention of the visitors, their influence on health, civilization, commerce and the industries, and as contributions to other investigations.

The necessity for study in the many divisions of pharmacy, the large number and varied forms of legislation, have contributed to education and legislation, and will be represented in the exhibit by a library of books and documents. This will again exemplify the many points of contact which have distinguished pharmacy in its many contributions to science, art and industry.

PARTICIPATION BY STATES IN THE HEADQUARTERS BUILDING.

THE American Pharmacy Headquarters Building will be completed before the end of 1933, and the thought is offered that all states will want to be represented in some way, perhaps illustrative or commemorative of pharmacy in the respective states. There is no intention of being definite, the subject is mentioned only because the associations may wish to consider the matter at the annual state meetings.

One of the purposes of the organization of the AMERICAN PHARMACEUTICAL ASSOCIATION was to encourage the establishment of state organizations to discuss the problems of pharmacists in the respective states at the annual meetings of the AMERICAN PHARMACEUTICAL ASSOCIATION, now possible in a larger way in the House of Delegates. The relationship brought about more than eighty years ago will, doubtless, grow stronger and more effective.

All states through individual and other contributions have shown their interest and attachment. The Headquarters should have a liberal endowment and such a contact is suggested for discussion at the annual conventions.

The building is located on the most beautiful site in Washington and is receiving frequent publicity in the daily press and in Government promotions. The progress of the building has been shown in recent issues of the JOURNAL, and the reports of Chairman H. A. B. Dunning have been published in the October and November numbers.

The British Pharmaceutical Society contemplates displacing its old building, which has served the Society for many years, by a new home. Just as a matter of interest, a unique presidential chair is being made of Australian woods for the building, to be presented to the British Pharmaceutical Society by the pharmaceutical organizations of Australia, New Zealand and Tasmania. The inlay woods represented are native to, and donated by New Zealand, Queensland, New South Wales, Victoria, South Australia, Tasmania and Western Australia.

NARCOTIC LEGISLATION.

SENATOR J. J. Davis, on January 3rd, introduced a bill "to provide for the forfeiture of vessels, vehicles or other means used to transport or conceal unstamped narcotics or to facilitate the purchase and sale thereof and for other

purposes." The Senator stated that he had introduced the bill on account of the growing difficulty of frequent forfeitures of automobiles and that unless proper provision is made the time is not far distant when such a seizure will be a useless proceeding—unless steps are taken to secure legislation to cure the defects in the present law, or, to enact a new law giving the Bureau of Narcotics authority to initiate proceedings looking to the forfeiture of all means used for the transportation or concealment of narcotics not bearing appropriate internal revenue tax stamps. Unless a step of this kind is taken the Senator states that one of the strongest curbs against the traffic will be taken away. The bill referred to is S. 5318.

The AMERICAN PHARMACEUTICAL ASSOCIATION, long before state and national legislation was enacted, interested itself in legislation to control the sale of narcotics.

The Senator referred to an item in the *Japan Advertiser* of September 21, 1932, informing that the Manchukuo government has promulgated provisional regulations governing the sale of opium for smoking purposes to the general public. It seems very unfortunate that such a means of revenue should be deemed necessary in this present day, when the destructive effects of narcotic addiction on an individual and nation are known.

It is gratifying to note that Kemal Pasha presided at a cabinet meeting on Christmas Day at which it was decided—that three recently closed narcotic factories in Istanbul will not be allowed to reopen; that poppy cultivation will be limited to meet the medicinal opium needs; that Turkey will adhere to the international accords of the Hague and Geneva for control of narcotic traffic and that special tribunals will be created to try narcotic smugglers and illegal manufacturers.

The Cabinet decree closed with the statement, "Thus we accomplish our most modern and most civilized duty toward the Turkish nation and humanity." This action is significant because in the past two years the unfortunate victims of narcotic traffic have been largely supplied from drugs which were the output of the three factories closed by the President of Turkey.

The United States was the first government to ratify the Geneva limitations' convention of 1931, which has since that time been ratified by Canada, Persia, Poland, Portugal and Sweden. Twenty-five countries must ratify before April 1933, to put the convention into force. Of these, four of six narcotic drug manufacturing nations must have ratified: England, Germany, France, Switzerland, Holland and the United States. The United States has ratified the convention.

The most recent work on adjustment of narcotic enforcement is the draft of a uniform drug act for states, prepared under the direction of the National Conference of Commissioners on Uniform State Laws. The final draft will go to the governors and legislatures of the several states; this, with certain comments and recommendations of a special committee of the National Drug Trade Conference, approved by the latter, has been mailed to state and national associations for careful consideration before the draft is considered for enactment. Pharmacists will recognize the importance of the comments and recommendations submitted and that the time to perfect the measure is before it becomes a law.

Preliminary education and training determines the quality of entrants to Pharmacy Schools—the work in the latter will characterize Pharmacy.

SCIENTIFIC SECTION

BOARD OF REVIEW ON PAPERS.—*Chairman*, L. W. Rowe; John C. Krantz, Jr.; F. J. Bacon.

THE ASSAY AND DETERIORATION OF ERGOT PREPARATIONS.

BY O. F. SWOAP, G. F. CARTLAND AND M. C. HART.

The knowledge that ergot and its extracts deteriorate more or less rapidly is not new although it has only comparatively recently been clearly established by the application of newer and more accurate methods of assay. A great many of the studies on the deterioration of ergot have been made on specimens prepared in the laboratory. Thompson (1) and others have suggested that Fluidextracts of Ergot prepared on a small scale in the laboratory may differ in potency and stability from lots prepared on a manufacturing scale. The work here reported represents a two years' study of manufacturing methods, assay methods and standards as applied to ergot extracts made on a manufacturing scale.

As a result of these studies we have concluded that either of the assay methods used in this work is superior to the present Official Cockscomb Method for control of Fluidextract of Ergot. It is also our conclusion that no method of manufacture at present available will yield a Fluidextract of Ergot which is permanently stable. Since it is obvious that frequently opened and partially filled specimens of Fluidextract of Ergot deteriorate much more rapidly than unopened, completely filled bottles, it is important that Fluidextract of Ergot should pass from the manufacturer to the patient in an unopened package. With the possible exception of that intended for use in the large hospitals, Fluidextract of Ergot should be packaged only in one-ounce containers.

EXPERIMENTAL.

Methods of Assay.—The Cockscomb Method official in the U. S. P. X is unsuitable for studying changes in ergot and its extracts. Consequently the Rabbit Uterus Method of Broom and Clark (2) and the Chemical Colorimetric Method of Smith (3) have been used in this work. Of the various modifications which have been suggested for the Rabbit Uterus Method as originally described by Broom and Clark, we have used that described by Pattee and Nelson (4).

The Chemical Colorimetric Method as described by Smith has been slightly modified as follows: The removal of alcohol from the Fluidextract has been omitted since the alcohol does not interfere with the extraction and is of value in aiding the separation of emulsions. The ether solution of the alkaloids is not made up to volume and divided into aliquots as described by Smith, but, on the contrary, the entire ether extract from 5 cc. of Fluidextract is extracted with 1% tartaric acid. During the addition of the paradimethylaminobenzaldehyde reagent heating has been avoided by immersing the tubes in cold water. For the development of color we have used a Hanovia Mercury Lamp No. AC 154 at a distance of 18 cm. Parallel assays made using these modifications and by the exact technic as described by Smith have yielded identical results. Since sunlight and the lamp used as sources of light have yielded identical results, we have adopted the lamp due to its greater dependability.

Crystalline ergotamine tartrate has been used as a standard and all results are reported in mg. equivalent of ergotamine tartrate per cc. of fluids or per Gm. of solids. The standard has been dissolved in 1% tartaric acid solution to make a concentration of 1 mg. per cc., filled into ampuls and kept in a refrigerator. The standard has been freshly prepared every three months and has been checked against a similar solution prepared by Dr. M. I. Smith.

Deterioration of Fluidextract of Ergot.—Thirteen lots of Fluidextract of Ergot prepared on a manufacturing scale by the U. S. P. X process were assayed at three-month intervals over a period of one year. The results are summarized in Table I.

TABLE I.—CHANGES IN FLUIDEXTRACTS OF ERGOT AS RECORDED BY THE COLORIMETRIC AND BROOM-CLARK METHODS OF ASSAY.*

Fluidextract No.	Initial Assay. Color.	B-C.	3 Months. Color.	B-C.	6 Months. Color.	B-C.	9 Months. Color.	B-C.	12 Months. Color.	B-C.
82158	0.60	0.60	0.41		0.32	0.20	0.15		0.10	0.10
82528	0.63	0.60	0.63		0.50	0.50	0.33		0.14	0.13
Do. unopened	0.63	0.60							0.61	0.50
82799	0.66	0.60			0.58		0.27		0.14	0.15
Do. unopened	0.66	0.60							0.39	0.35
83173	0.69	0.65	0.59		0.57		0.33		0.22	0.15
Do. unopened	0.69	0.65							0.38	0.35
83504	0.73	0.70	0.52		0.47		0.34		0.21	0.10
83772	0.63		0.63		0.44		0.29		0.12	
Do. unopened	0.63								0.49	
83857	1.00	1.00	0.86		0.69	0.65	0.42		0.25	
Do. unopened	1.00	1.00							0.85	0.70
84052	0.87	1.00	0.89		0.64	0.50	0.47		0.24	0.15
Do. unopened	0.87	1.00							0.67	0.40
84165	1.60		1.29		1.18	1.00	0.72		0.38	0.33
Do. unopened	1.60								1.05	0.90
84166	1.55	1.20	1.28		1.22	0.75	0.65		0.32	0.30
Do. unopened	1.55	1.20							1.00	0.95
84247	0.80	0.87	0.59		0.58	0.33	0.42		0.21	0.16
84248	1.17	1.25	0.97		0.90	0.70	0.61		0.27	0.25
84312	0.82		0.77		0.75		0.63		0.34	

* Amber bottles were completely filled after the initial assays and aliquots were removed at 3-month intervals for assay. In some cases parallel assays were made at the end of one year on unopened specimens. All results are reported in mg. equivalent of ergotamine tartrate per cc.

Those samples which were opened at three-month intervals for removal of aliquots for assay show at the end of one year an average deterioration of 75% by the Colorimetric Method and 80% by the Broom-Clark Method. The unopened samples at the end of one year show an average deterioration of 27% by the Colorimetric Method and 36% by the Broom-Clark Method. This demonstrates very clearly the harmful effect of only occasionally opening and removing part of the contents from a bottle of Fluidextract of Ergot. The individual variations in stability are very great. For example, of the eight unopened samples assayed at the end of one year by the Colorimetric Method, the most stable had lost only 3% and the least stable had lost 45% of its potency.

The agreement between the Colorimetric and Broom-Clark Methods is good in the case of newly manufactured fluidextracts. Of the ten fluidextracts for which

initial assays were made by both methods, only two (84052 and 84166) show a discrepancy of greater than 10%. The one showing the greatest discrepancy (84166) is one in which the initial color assay is very high.

Although both methods indicate the rate of deterioration, a poorer agreement between the two methods is observed in the older fluidextracts which have undergone deterioration. In almost every case where the two methods show a disagreement, the Broom-Clark Method has yielded lower results than the Colorimetric Method. Thus a preparation which tests low by the Colorimetric Method has, in our experience, invariably tested low by the Broom-Clark Method, but the reverse is not necessarily true. Since the biologically inactive alkaloids of ergot are active in producing color, our results would indicate that as Fluidextract of Ergot deteriorates the disappearance of active alkaloids is likely to be greater than that of the inactive alkaloids. We have no evidence, however, that the biologically active alkaloids are converted into inactive alkaloids during the process of deterioration. That such a conversion can occur is indicated by an experiment of Wokes and Crocker (5) in which an 18 months old ergotoxine phosphate solution was found by Colorimetric assay to have 66% of its original activity and by Broom-Clark assay only 10% of its original potency. Such a change as this can only be explained on the basis of a conversion of active into inactive alkaloids.

Wokes and Crocker (5) have severely criticized the Colorimetric Method of Smith because it measures the inactive as well as the active alkaloids. However, the biologically inactive alkaloidal content of Fluidextract of Ergot prepared on a manufacturing scale is seldom high enough to interfere significantly with the Colorimetric Method in measuring biological potency. Consequently the method is of great value in controlling the manufacturing process. But in view of the fact that occasionally a lot of ergot is encountered which is high in the inactive alkaloids it is well to check the potency of the finished extract by the Broom-Clark Method.

TABLE II.—CHANGES IN FLUIDEXTRACTS OF ERGOT AS AFFECTED BY ADJUSTMENT OF p_H.*

Fluidextract No.	Initial. Color.	Initial. B-C.	3 Months. Color.	3 Months. B-C.	6 Months. Color.	6 Months. B-C.	9 Months. Color.	9 Months. B-C.	12 Months. Color.	12 Months. B-C.
81889										
Natural p_H 4.7	0.51	0.38	0.44		0.35	0.25	0.29		0.24	0.20
Do. adjusted p_H 3.0	0.51	0.38	0.39		0.29	0.15	0.19		0.13	0.10
Do. adjusted p_H 6.1	0.51	0.38	0.39		0.29	0.08	0.09		0.07	0.05
82712										
Natural p_H 4 6	0.61	0.65	0.60		0.55		0.54		0.45	0.33
Do. adjusted p_H 3.0	0.61	0.65	0.55		0.54		0.49		0.41	0.22
Do. adjusted p_H 6.1	0.61	0.65	0.48		0.43		0.38		0.28	0.15
87380										
Natural p_H 4.6	0.81				0.57					
Do. adjusted p_H 3.0	0.81				0.36					

* The conditions of storage and assays are the same as for the fluidextracts reported in Table I. Results reported in mg. equivalent of ergotamine tartrate per cc.

Effect of p_H Adjustment upon the Stability of Fluidextract of Ergot.—Three lots of Fluidextract of Ergot prepared by the U. S. P. X process were found to have a p_H of 4.6–4.7. Aliquots were adjusted to a p_H of 3.0 by the addition of hydrochloric acid and to a p_H of 6.1 by the addition of sodium hydroxide. Assays made immediately after the p_H adjustment show that no loss of alkaloidal potency occurred during the addition of acid and alkali. However, later assays, summarized in Table II, indicate that this adjustment of p_H had an unfavorable effect upon the stability of the extracts. The samples with a p_H of 3.0 are in every case less stable than the unadjusted sample and the two samples adjusted to a p_H of 6.1 are the least stable of all.

In his earlier work Swanson (6) concluded that a p_H of 3 or less is necessary for the stability of Fluidextract of Ergot. However, more recently, Swanson (7) *et al.*, somewhat modifies his former conclusions. Smith and Stohlman (8) conclude that variation of p_H from 5.2 to 2.2 does not favor the stability of Fluidextract of Ergot.

Our conclusions are that variation of p_H between the limits of 3.0 to 6.1 does not enhance the stability of Fluidextract of Ergot. Manipulation of p_H in the finished fluidextract appears to be more harmful than beneficial.

Changes in Fluidextracts of Ergot as Affected by Frequent Opening of the Bottle for Removal of Part of the Contents.—The results summarized in Tables I and II indicate the extremely rapid deterioration of samples which are opened at three-month intervals. The conditions under which this deterioration occurs are not essentially different from those under which Fluidextract of Ergot is dispensed. The physician or druggist who buys this preparation in pint or gallon containers is compelled to subject the contents to opening at intervals considerably more frequent than three months.

In order to study the effects of such manipulation two lots of Fluidextract of Ergot were set aside in large bottles. They were opened once every two weeks and one ounce of the contents removed. At the end of six months, assays on the remainder of the contents showed a loss of 76 and 74% of the original alkaloidal potencies. Control, unopened samples of the same lots assayed in parallel were found to have lost only 14 and 3%, respectively, of their original potencies.

These results confirm those reported above in showing that under conditions of frequent opening and partial removal of the contents, Fluidextract of Ergot may become practically inactive in only a few months. This rapid deterioration can be greatly reduced, although not completely eliminated if the manufacturer will package Fluidextract of Ergot only in one-ounce containers, which will reach the consumer in an unopened condition.

Attempts to Stabilize Fluidextract of Ergot by Bottling under Different Gases.—Since Fluidextract of Ergot deteriorates rapidly when frequently exposed to the air, the question arose as to whether a stabilization could be accomplished by excluding air at the time of bottling. Samples from a single lot of fluidextract were bottled in one-ounce amber bottles under air, nitrogen, carbon dioxide and oxygen. The oxygen samples were treated with a vigorous stream of oxygen for two hours before being stoppered. This resulted in only a slight immediate loss of potency as measured by the Colorimetric Method but promoted a very rapid subsequent deterioration. The CO_2 samples were saturated with this gas before being

stoppered. In this entire series a new, unopened bottle was taken for each assay, and the relative stabilities of the groups are summarized in Table III.

TABLE III.—CHANGES IN FLUIDEXTRACT OF ERGOT AS AFFECTED BY BOTTLING UNDER DIFFERENT GASES.*

Fluidextract.	Initial. Color.	B-C.	3 Months. Color.	B-C.	6 Months. Color.	B.-C.	9 Months. Color.	B-C.	12 Months. Color.	B-C.
Under air	1.30	1.00	1.05		0.85	0.65	0.73		0.70	0.55
Under N_2	1.30	1.00	0.99		0.92	0.75	0.65		0.18	0.20
Under CO_2	1.30	1.00	1.10		0.78	0.60	0.77		0.71	0.60
Under O_2	1.20	1.00	0.47		0.33	0.20	0.24		0.21	0.15

* All assays made on previously unopened specimens. Results reported in mg. equivalent of ergotamine tartrate per cc.

As would be expected, the oxygenated fluidextract proved to be the most unstable of the series. The fluidextracts bottled under nitrogen and carbon dioxide are no more stable than those bottled under air in the usual way. We are unable to account for the rapid deterioration of the nitrogen sample during the last three months of the test. This sample was assayed at twelve months on three different bottles with identical results. Consequently it is not a condition peculiar to a single bottle of the nitrogen series.

Although oxidation is probably an important factor in the deterioration of ergot alkaloids, our attempts at stabilization of the fluidextract by the exclusion of air and bottling under an inert gas have been unsuccessful. Similarly the attempts of Rowe and Scoville (9), Smith and Stohlman (8), and Powell, Schulze and Swanson (10) to stabilize Fluidextracts of Ergot by the use of reducing agents and buffers have yielded irregular and inconclusive results.

The Deterioration of Amine-Free Fluidextracts of Ergot.—Thompson (11) has developed a process for manufacturing a Fluidextract of Ergot in which the amines are removed by a preliminary extraction with weak alkali. The chief advantage of such an extract over the regular U. S. P. product appears to be that removal of the interfering amines eliminates one of the many sources of error in standardizing the Fluidextract by the Cockscomb Method.

In order to determine whether the removal of amines increases the stability of Fluidextract of Ergot, four lots were prepared by Thompson's method and studied over a period of one year. By both the Colorimetric and Broom-Clark Methods of assay these were found to be no more stable than the regular U. S. P. Fluidextracts reported in Table I. Consequently we conclude that the removal of amines does not lessen the deterioration of Fluidextract of Ergot.

The Stability of Powdered Extracts of Ergot.—Powdered extracts of ergot have been prepared on a manufacturing scale by concentrating the fluidextract to dryness *in vacuo*. This process requires prolonged heating which is known to have an adverse effect upon the stability of Fluidextract of Ergot. By such a process the yield has been found to be from 70 to 90% of the alkaloidal potency of the fluidextract used as starting material. Three lots of powdered extract of ergot prepared in this way have maintained their potency without detectable loss over a period of one year. These samples were stoppered in amber and flint bottles and assayed by both the Colorimetric and Broom-Clark Methods. Our findings are in agreement with those of Oettel (12) who reports that dry extracts of ergot show

no loss of potency during a period of eight months in contrast to a loss of two-thirds of the potency occurring during the same period in the fluidextracts from which the dry extracts were prepared. Thus, we conclude that the dried extract of ergot is the most stable crude alkaloidal preparation thus far obtained and stands in marked contrast to the instability of crude ergot and its fluidextract.

Consideration of Standards.—The standard Fluidextract of Ergot which has been official in the U. S. P. X is unsatisfactory because of its instability. Although ampuled *in vacuo*, the most recent official standard No. 2160 is no more stable than many market samples of Fluidextract of Ergot. Our assays have shown that the standard Fluidextract No. 2160 has shown a progressive loss of potency amounting to 43% by the Broom-Clark Method and 37% by the Colorimetric Method during a period of 20 months.

Crystalline ergotamine tartrate and ergotoxine ethanesulphonate have both been suggested as ergot standards. Either of these is apparently stable in the dry form if protected from air, moisture and light, and offers a marked improvement over the present fluidextract standard. Solutions of these salts in 1% tartaric acid when ampuled and kept in a refrigerator are stable for at least six months. As a result of numerous assays we conclude that ergotamine tartrate (Sandoz) and ergotoxine ethanesulphonate (Burroughs, Wellcome and Company) are equivalent by the Colorimetric Method, but by the Broom-Clark Method one mg. of ergotoxine ethanesulphonate is equal to 1.25 mg. of ergotamine tartrate.

Consequently, the use of the ergotoxine salt as a standard for assaying Fluidextract of Ergot will tend to cause a 25% disagreement between the Broom-Clark and Colorimetric Methods of assay.

SUMMARY.

The more or less rapid and variable deterioration of Fluidextract of Ergot has been confirmed. Since frequent opening and exposure to air is inducive to an extremely rapid deterioration, it is recommended that Fluidextract of Ergot be put up in small unit packages to insure transfer to the patient in the original, unopened container. Adjustment to a p_H of 3.0 or removal of amines does not increase the stability of the fluidextract. The powdered extract appears to be the most stable crude ergot preparation.

The chemical Colorimetric Method of Smith gave results agreeing sufficiently closely with the Broom-Clark Biological Method to make it extremely valuable for controlling the manufacture of Fluidextract of Ergot. Either of these methods is superior to the Cockscomb Method. Either crystalline ergotamine tartrate or ergotoxine ethanesulphonate will make a much more satisfactory standard than the present unstable standard fluidextract.

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STUDIES IN THE EXTRACTION AND HYDROGEN-ION CONCENTRATION OF TINCTURE OF DIGITALIS.

BY JOHN C. KRANTZ, JR., AND JAMES C. MUNCH.

INTRODUCTION.

In a previous communication to THIS JOURNAL the authors (1) studied the relationship between the potency and the hydrogen-ion concentration of tincture of digitalis. In this investigation it was shown that the tincture prepared with dehydrated alcohol as a menstruum, differed from that tincture prepared with 80 per cent in at least three respects. *First*, the tincture prepared with dehydrated alcohol showed a greater hydrogen-ion concentration, *second*, a comparatively negligible amount of ash was present and *third*, the heart tonic value was markedly less than that exhibited by the tincture prepared from the same drug with 80 per cent alcohol.

Since the publication of this work, the comprehensive investigations of Hoekstra (2) have come to the authors' attention. Among other interesting observations, this investigator showed that a tincture prepared with 50 per cent alcohol contained 3.8 cat units of digitoxin, 2.5 cat units of gitalin and 7.3 cat units of bigitalin. Whereas a tincture prepared from the same powder using dehydrated alcohol as a menstruum contained $^3/_8$ the digitoxin content, $^5/_8$ the total bigitalin content and only a trace of gitalin. Wokes (3), after a study of the potency and total solids of tincture of digitalis, concluded that no definite relationship could be established between these factors. Of striking significance is the observation of Stasiak and Zboray (4) who found less residues from the tinctures made with dehydrated alcohol than those prepared with diluted alcohol. In addition, the tincture prepared with dehydrated alcohol showed the lowest potency when assayed by the cat method, but by the frog method the tinctures prepared with dehydrated 70 per cent and 50 per cent alcohol, showed essentially the same potency.

In this study the authors have extended their investigations mentioned in a foregoing paragraph and attempted to correlate their findings with the work of other workers.

EXPERIMENTAL.

Through the courtesy of the Upsher Smith Company and Penick Company, six authenticated samples of digitalis (*purpurea*) were obtained. From these, six tinctures were prepared by the official method. The removal of fat was omitted. Six tinctures were prepared using dehydrated alcohol as a menstruum and from the marcs obtained in this extraction six other tinctures were prepared using 80 per cent alcohol as a menstruum.

The hydrogen-ion concentration of these tinctures was measured by the hydrogen electrode Wilson (5) type. The results were reproducible within 0.1 unit p_H. The ash and acid-insoluble ash of the drugs were determined as well as the ash of the tinctures. The tinctures were assayed for digitoxin by a slight modification of the Keller-Fromme (6) method. In addition the preparations were assayed colorimetrically by the Knudson-Dresbach (7) method using a ouabain standard, and also by the U. S. P. one-hour frog method.

Very recently Dyer (8) critically studied the Knudson-Dresbach method and concluded that the results obtained did not parallel those obtained by the frog method.

The results are shown in Tables I, II and III.

TABLE I.—THE ASH OF DIGITALIS AND ITS TINCTURE.

No.	Drug Ash Per Cent.	Drug Ash Insoluble in HCl Per Cent.	Drug Ash Sol. in HCl Per Cent.	Ash in Tinct. Mg. per L. U. S. P.	Ash in Tinct. Mg. per L. Dehydrated Alcohol.	Ash in Tinct. Mg. per L. Re-extraction.
1	12.75	5.35	7.40	2850	380	1910
2	7.34	0.16	7.18	2430	280	1450
3	7.76	0.06	7.70	2300	280	1310
4	8.59	0.80	7.79	2720	360	1570
5	7.40	0.11	7.29	2160	260	980
6	9.78	1.88	7.90	2760	400	1470

TABLE II.—THE HYDROGEN-ION CONCENTRATION OF TINCTURE OF DIGITALIS.

No.	U. S. P. Tincture, p_H.	Dehydrated Alcohol Tincture, p_H.	Re-extraction Tincture, p_H.
1	5.78	4.10	5.79
2	6.12	4.13	5.91
3	6.25	4.13	6.12
4	6.15	4.12	6.06
5	6.27	4.60	6.15
6	6.08	4.45	5.85

TABLE III.—ASSAYS OF TINCTURE OF DIGITALIS.[1]

		U. S. P. Method.	Knudson-Dresbach.	Keller-Fromme
1	U. S. P. Tincture	100	120	130
2	Dehydrated Alcohol Tincture	84	76	70
3	Re-extraction Tincture	30	100	70

[1] The assay-values are expressed in terms of per cent of potency compared with the U. S. P. standard. The Keller-Fromme standard of 30 mg. per 100 cc. was considered 100 per cent. For assay purposes all six tinctures extracted in the same manner were combined.

DISCUSSION OF RESULTS.

Hydrogen-Ion Concentration.—The results of these investigations on six additional samples of tincture of digitalis confirm the findings of the authors in their previous communication (1). Thus the average p_H of the U. S. P. tincture was found to be 6.11, the p_H of the tincture prepared with dehydrated alcohol 4.25 and the p_H of the tincture prepared by re-extraction 5.98. As it was suggested, this phenomenon is associated with the inorganic constituents of the leaf combined with the organic acids which were studied by Fourton (9). The analysis of the ash showed approximately 76 per cent of potassium carbonate. The U. S. P. tincture

contained approximately ten times more inorganic constituents than the tincture prepared with dehydrated alcohol. With the acids and inorganic constituents present, the U. S. P. tincture exhibits a high buffer capacity as shown by J. K. (10), whereas the tincture prepared with absolute alcohol is practically devoid of inorganic constituents. This is evinced by its low ash content, high hydrogen-ion concentration and low buffer capacity (11).

Nyiri and DuBois (12) showed that the nutrient fluid of the heart can be changed in hydrogen-ion concentration between p_H 5.2 and 7.6 without visible damage to the heart action. These investigators claim full digitalis action to take place only within this range of p_H. Accordingly hydrochloric acid was added to the U. S. P. tincture (1 cc. 0.1 *N* to 20 cc.) to change its p_H to approximately that of the tincture prepared with dehydrated alcohol. The p_H was determined and after six months' standing the biological potency was determined by the U S. P. method. The results are shown in Table IV.

TABLE IV.—POTENCY OF ACIDIFIED TINCTURE OF DIGITALIS.

No.	p_H	Potency Frog Method—Per Cent.
1	3.83	63
2	4.12	53
3	4.13	79
4	3.94	47
5	3.93	58
6	4.09	58

The average potency of the acidified tincture is approximately 60 per cent of that of the unacidified preparation. The authors are not at present in a position to attribute this loss in heart tonic value to a change in p_H *per se* or the influence which the more acidic preparation might exert on the nutrient fluid of the heart. The indications are that the former condition obtains, as it is well known that upon long standing tinctures of digitalis decrease in potency and increase in hydrogen-ion concentration simultaneously (13), (14), (15), (16).

Ash Content.—The ash content soluble in hydrochloric acid of the six samples of drug was quite uniform, although the total ash content varies from 7.34 to 12.75 per cent. It is interesting to note that Specimen "1" with 12.75 per cent is Minnesota grown digitalis and Specimens 2, 3, 4 and 5 are Canada grown digitalis. The source of Specimen 6 is unknown. Newcomb and Haynes (17) found eleven samples of digitalis gathered personally to vary in ash content from 6.6 to 14.4 per cent.

The influence of the potassium ion in the ash as a factor affecting biologic potency was studied. Solutions of potassium chloride 2500 mg. per liter had no effect on the frog's heart when injected in quantities up to 24 cc. per kilogram. Large doses of a concentrated solution of potassium chloride caused heart stoppage in systole similar to oubain and digitalis. To produce this 2500 mg. per kilogram of a 10 per cent solution of potassium chloride were necessary.

From this it seems evident that the potassium ion as such is not directly responsible for the cardiac response in the re-extraction tincture which contains a relatively large amount of ash. Further, it does not seem to indicate that the deficiency of heart tonic value of the tincture prepared with dehydrated alcohol is due to the small quantity of ash present.

Biological Potency.—Table III shows a comparison of the composite tinctures assayed by three methods. The U. S. P. tincture contained 39.1 mg. of digitoxin per 100 cc., the tincture prepared with dehydrated alcohol 21.0 mg. per 100 cc. and the re-extraction tincture 20.9 mg. per 100 cc. The incapacity of dehydrated alcohol to extract this glucoside by the ordinary process of percolation is indicated by these results and substantiated by the U. S. P. and Knudson and Dresbach methods. The wide discrepancies in the results obtained by the three methods on the re-extraction tincture are exceedingly interesting. In the experiments reported previously by the authors, the re-extraction tinctures showed an average potency of 58 per cent of that by the U. S. P. method. Yet by the Knudson-Dresbach, seven assays of the composite sample showed a potency of 83 per cent of that of the U. S. P. tincture assayed by this method.

The digitoxin extraction (Keller-Fromme) method and the U. S. P. method indicate that the heart tonic value of the U. S. P. tincture is distributed, within the limits of the error of the experiment, between the dehydrated alcohol tincture and the re-extraction tincture. However, the ratio of distribution is vastly different as indicated by the two methods.

Further experimental work will be necessary to determine the rôle of these inorganic constituents found in the U. S. P. tincture, re-extraction tincture and absent in the dehydrated alcohol tincture and pharmacologic activity of the digitalis glucosides in these preparations. In view of the fact that the acidifying of the U. S. P. tincture with hydrochloric reduced materially its potency (Table IV) seems to indicate that the acid-base equilibrium of the tincture is a criterion of potency as measured by the U. S. P. method.

SUMMARY.

1. A greater degree of hydrogen-ion concentration in tinctures of digitalis prepared with dehydrated alcohol than those prepared with 80 per cent alcohol has been established.

2. The ash content of the tinctures prepared with dehydrated alcohol has been shown to be negligible compared with that of the tincture extracted with 80 per cent alcohol.

3. Work of other investigators has been substantiated indicating the inefficiency of dehydrated alcohol as a solvent for digitalis.

4. No conclusions can be drawn as yet regarding the pharmacological rôle of the inorganic constituents of the leaf present in the tincture.

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ALCOHOL-SOLUBLE EXTRACTIVE OF BENZOIN, MYRRH AND ASAFŒTIDA.

BY B. V. CHRISTENSEN.*

There has been considerable complaint regarding the present U. S. P. method for determining the alcohol-soluble extractive of some drugs because of the loss of volatile constituents during the drying of the extract. This criticism applies particularly to Benzoin, myrrh and asafœtida. Of these, the one that apparently has been causing the most trouble is benzoin. It is suggested by Bickford and Bennett that the alcoholic extractive, including the water, be obtained by means of a Soxhlet extraction apparatus and that the water content be determined by the Xylol method. Other modifications of the U. S. P. method have been proposed but while they appear to give results which probably indicate a truer figure than the U. S. P. method, they are long and tedious and subject to other criticisms as well.

In this investigation there are, therefore, three questions involved, namely: *First*, is the proposed new method (Soxhlet and Xylol) for the determination of alcohol extractive reasonably speedy and satisfactory in that it gives concordant results? *Second*, is the proposed method suitable for other U. S. P. drugs such as, asafœtida and myrrh? *Third*, are these drugs as they occur in commerce at present, meeting the alcohol-soluble extractive requirements of the U. S. P.?

The method (No. 9) proposed by Bickford and Bennett is as follows:

> "Weigh 2 Gm. of the sample into a dried and tared paper extraction thimble, using a glass stopper weighing bottle as a container. Extract in a continuous extraction apparatus with 95% alcohol containing about 0.5 Gm. NaOH for 5 hours. Dry and weigh thimble and calculate alcohol extractive matter plus water by difference. Deduct water as determined by xylol distillation method from the result and report as alcohol extract."

Below is a report of a brief study of this method as compared to the U. S. P. method.

Preparation of Samples.—Samples of Siam benzoin, sumatra benzoin and myrrh, consisting of about one pound each, were ground in a mortar and quartered. One quarter was further reduced to a No. 20 powder and used for analysis. In the case of asafœtida about one pound was broken up into small particles and quartered. One quarter was then used for analysis.

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Methods.—See U. S. P. X, page 466, for Siam benzoin, Sumatra benzoin and myrrh; U. S. P., page 67, for Asafœtida; and Bickford and Bennett method No. 9 as described in the foregoing.

TABULATION OF RESULTS.

Method.		Sumatra Benzoin.	Siam Benzoin.	Myrrh.	Asafœtida.
U. S. P. X		73.59%	89.80%	31.40%	55.44%
		73.20	90.90	31.10	54.74
	(Average)	73.39	90.35	31.25	55.09
No. 9		77.10	94.10	37.00	10.20
		78.50	94.30	36.80	13.30
	(Average)	77.80	94.20	36.90	11.75
Xylol Method (Moisture)		5.60%	1.90%	11.30%	7.60%

COMMENTS.

In checking the time required to make these determinations, it was found that with the U. S. P. method the process extended through an interval of from 26 to 30 hours, while for B. &. B. No. 9 from 7 to 9 hours were required, providing the moisture determinations were carried out concurrently with extraction, which is easily done. It is possible that this might be further reduced by limiting the extraction to 3 hours. In the case of the benzoin and myrrh the solvent appeared to be perfectly clear at the end of 2 hours, but this, of course, is a point to be determined by further experimentation.

While the U. S. P. method gives figures in the case of the Siam benzoin, myrrh and Asafœtida tested that meet the U. S. P. requirements, it is to be noted that the figures obtained by method No. 9 are consistently higher except for asafœtida. Inasmuch as this indirect method obviates the question of volatile matter, these figures are probably more nearly true, except for asafœtida, than those obtained by the U. S. P. method.

While the U. S. P. method for asafœtida is both tedious and cumbersome it appears, however, to give figures which meet the standard. Method No. 9 is not applicable with asafœtida in lumps as permitted by the U. S. P. method. Possibly if it were reduced to a powder by using purified sand, method No. 9 would give more consistent results. This, of course, would introduce another possibility for error but it appears that it is worth trying at least.

The limited observations covered by this report suggests that the method proposed by Bickford and Bennett is applicable to Siam benzoin, Sumatra benzoin and myrrh, and is to be commended for speed, accuracy and simplicity.

It is suggested that experimentation along this line be continued with enough commercial samples of these drugs to furnish sufficient data from which definite conclusions may be drawn.

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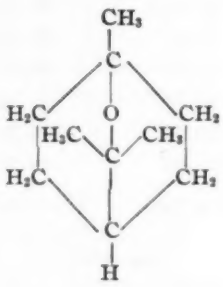
E. N. Gathercoal, personal letters.

NEW MOLECULAR COMPOUNDS OF EUCALYPTOL.

BY FRANCIS D. DODGE.*

Cineol, or eucalyptol, as it is more generally called, a cyclic ether having the formula:



is remarkable for the variety of molecular compounds which it forms with acids, phenols and salts. A list of these has been given by Muller.[1]

The acids which so far have been found to yield crystalline compounds are: HCl, HBr, HI, H_3AsO_4, H_3PO_4, ferro- and ferricyanic, cobalti- and platinocyanic, oxalic and ortho-coumaric acids, and the arsenic and phosphoric compounds have been utilized for the determination of eucalyptol in the various oils of which it is a constituent.

Phenol compounds have been obtained with phenol, the three cresols: catechol, resorcinol and hydroquinone; pyrogallol, thymol, alpha and beta naphthol; the resorcinol and ortho-cresol compounds have also found application in analytical methods.

Other compounds not listed by Muller are those with 1.5 dioxy-naphthalene,[2] and with meta-nitro-benzaldehyde.[3]

The list of phenolic compounds, however, appears to be by no means exhausted, and has been extended a little by the addition of the following, prepared by the writer.

Eucalyptol and Ortho-Chlor-Phenol.—On dissolving 6 Gm. *o*-chlor-phenol in 20 Gm. warm eucalyptol, the compound crystallized in large prisms, on cooling. Melting point: 57–59°. Analysis: 6.667 Gm. dissolved in an excess of 10% NaOH, in a "cassia" flask, yielded eucalyptol, 3.6 Gm. or 54%. (Calc. for $C_6H_4ClOH.C_{10}H_{18}O$, 54.5%.)

Eucalyptol and Ortho-Brom-Phenol.—Five grams *o*-brom-phenol, dissolved in 20 Gm. eucalyptol, yielded about 8 Gm. of transparent prisms, melting at 75.5–76° (uncorr.). Analysis: 1.903 Gm., dissolved in 5 ml 10% NaOH, yielded 0.88 Gm. eucalyptol, or 46.2%. (Calc. for $C_6H_4BrOH.C_{10}H_{18}O$, 47.1%.)

Eucalyptol and Ortho-Iodo-Phenol.—Preparation as in the case of *o*-brom-phenol. Yield 7.5 Gm. Melting point: 89–89.5° (uncorr.). Analysis: 1.889 Gm. yielded 0.739 eucalyptol, or 39%. (Calc. for $C_6H_4IOH.C_{10}H_{18}O$, 41.1%.)

The three compounds are thus analogous in composition to the ortho-cresol compound.

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* Scientific Section, A. PH. A., Toronto meeting, 1932.

[1] *Riechst. Ind.*, 4 (1929), 143.

[2] *Pharm. Zentr.* (1912), 32.

[3] *Centr. Bl.*, 1 (1893), 657.

Eucalyptol and Para-Hydroxy-Benzoic Acid.—Preparation like the previous compound. Yield, about 7 Gm. of long prisms which lose eucalyptol rapidly on exposure, and melt, with decomposition, at 63–65°. Analysis: 2.29 Gm. dissolved in alcohol required 10.8 ml 0.5 *N* KOH, equivalent to 0.745 Gm. *p*-hydroxy-benzoic acid, or 32.5%. (Calc. for $C_6H_4OH.COOH.C_{10}H_{18}O$, 47.2% acid. Calc. for $C_6H_4OH.COOH.2C_{10}H_{18}O$, 30.9% acid.)

The analysis is not very exact, owing partly to the ready dissociation of the compound, and also to the fact that the acid yields high figures on titration, due to the presence of the hydroxyl group. The conclusion, however, appears justified, that the compound is analogous to those with resorcinol and hydroquinone, which contain two molecules of eucalyptol to one of the phenol.

The preparation of molecular compounds with tri-brom-, tri-chlor-, tri-nitro-phenol; guaiacol, eugenol and isoeugenol; salicylic, meta-hydroxybenzoic, anisic, veratric, ortho-, meta-, para-nitrobenzoic or anthranilic acids; ortho- or para-hydroxy-benzaldehyde was unsuccessful.

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FURTHER OBSERVATIONS UPON THE BROMINE METHOD FOR THE ESTIMATION OF ALKALOIDS.

BY H. B. HAAG.*

Several years ago Weiss and Hatcher (1) described a method for the quantitative estimation of quinine and quinidine, both in pure solutions and in tissue extracts. The adaptability of this test depends upon the fact that these alkaloids promptly decolorize diluted bromine water by uniting chemically with the bromine with resulting disappearance of the yellow color.

This summer, while working in the Department of Pharmacology of Cornell University Medical College, New York City, the thought occurred that this procedure might be extended to include other common alkaloids and related compounds. The technic employed was essentially identical to that previously outlined by Weiss and Hatcher. Diluted bromine water was prepared by diluting a saturated aqueous solution ten times with distilled water. It was concluded from several tests that this diluted bromine solution, when kept in a glass-stoppered bottle, did not rapidly deteriorate and hence the freshly diluted preparation certainly retained, for purposes of this test, its original concentration for at least several hours. The standard solution of the alkaloid was prepared so that each cubic centimeter corresponded to 1.0 mg. of the alkaloidal base, and was made up in 0.5% sulphuric acid. In this connection it should be mentioned that all solutions tested against the bromine water should be acid, as alkalies themselves decolorize the solution. The bromine water was standardized against this known solution as follows: 0.5 cc. of the diluted bromine water, accurately measured, was placed in a test-tube of about 5 cc. capacity, and then the standard was gradually added from a micro-pipette until complete decolorization of the bromine water had taken place, as viewed by reflected light against a white background. This was repeated so that an average value could be obtained from several fairly

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concordant titrations. The solution of unknown concentration was then titrated in a similar manner and the calculations made by dividing the number of cubic centimeters of the standard solution necessary for the decolorization of 0.5 cc. of the diluted bromine water by the corresponding number for the unknown. The resulting figure represented the amount of alkaloid, in mg. in 1 cc. of the unknown solution. By employing such a procedure it was possible to estimate within 5 per cent of the concentration of unknown solutions.

The test is also applicable to tissue extracts upon which quantitative studies as to alkaloidal content are desired. In addition to quinine and quinidine mentioned by Weiss and Hatcher it was found that the following alkaloids, when present in a concentration of about 1–1000, lend themselves well to the test: ethylmorphine, diacetylmorphine, methylmorphine, cinchonidine, pilocarpine, strychnine, procaine, theobromine, caffeine, histamine, brucine, and to a limited extent, epinephrine. The following were found to be without influence upon the color of bromine water, and hence not suitable for the test: atropine, scopolamine, cocaine, betaine, sparteine, hydrastine, ephedrine and morphine. Physostigmine and papaverine first produced a white cloudiness which cleared upon the addition of a slight excess of the solution; whether practical use could be had in the case of these two is questionable. Apomorphine gave rise to a cherry-colored solution which did not decolorize. Nicotine had no decolorizing effect when used in a 1–1000 solution, but was quite effective in a concentration of 1 per cent.

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A METHOD OF DETERMINING A SMALL AMOUNT OF STRYCHNINE IN THE PRESENCE OF LARGER AMOUNTS OF QUININE AND CINCHONIDINE.*

BY GUSTAVE A. STICHT.

When the cinchona alkaloids are dissolved in an excess of hydrochloric acid, and these salts evaporated on a water-bath to dryness, until no more excess of acid is present, the so-called *di* salts are formed, and as is known, one-half of their acid radical is acid to methyl red when they are in solution, and both acid radicals are acid to phenolphthalein. Most other alkaloids, as strychnine, under the same treatment, only form salts that are neutral to methyl red, and acid to phenolphthalein. If a *di* acid and a *mono* acid alkaloidal salt are present together, then using methyl red and phenolphthalein indicators, the respective amounts of alkaloids can be estimated.

If the proportion of cinchona alkaloids to strychnine is not very large, and their acid radicals are combined as stated, then titrated as described below, the amounts of acid due to the cinchona alkaloid and strychnine, respectively, can be estimated with a fair degree of accuracy.

But in elixirs and such preparations, the amount of cinchona alkaloids is usually much larger than the strychnine, hence the bulk of the cinchona alkaloids must be separated. This is best done in the case of quinine and cinchonidine as a

* Scientific Section, A. PH. A., Toronto meeting, 1932.

tartrate. In the presence of the four cinchona alkaloids, quinine, cinchonidine, cinchonine, quinidine, and small amounts of strychnine, the estimation of the strychnine could be accomplished by successively precipitating quinine and cinchonidine as tartrate, cinchonine by its insolubility in ether, and quinidine as iodide. But the precipitations must be carried out in somewhat dilute solutions, to keep the strychnine from being co-precipitated. The method is rather tedious, because after each separation, the alkaloids in solution must be separated from the preponderance of salts, by chloroform and ammonia before being further manipulated. The precipitated alkaloids must likewise be treated with chloroform and ammonia if their determination is desired.

For convenience it is best to have at least one grain in the sample to be assayed, though smaller amounts have been determined.

The alkaloids are extracted from the measured or weighed sample by chloroform and ammonia, which solvent is evaporated or distilled off. When nearly dry, the residue is dissolved in an excess of dilute hydrochloric acid, with the aid of heat, the solution with its washings transferred to a dish of about 300 cc. capacity, and the rest of the chloroform is evaporated on a water-bath. The dish with its contents of about 100 cc. is placed over a small flame, some methyl red indicator added, and from a burette, dilute ammonia, about 5%, is very slowly added to the hot liquid, stirring at the same time, until the liquid is yellowish.

Sometimes, upon adding the dilute ammonia, small lumps of alkaloid are formed, mixed with the precipitated tartrate, which formation must be avoided. It is best then to re-dissolve the precipitate while solution is kept hot, by the careful addition of stronger acid, until all is dissolved again, and then once more adding the dilute ammonia as described above. The lumps are apt to form if the ammonia is added too rapidly, the solution of alkaloids is too concentrated, or the solution was not stirred sufficiently while neutralizing. Then from another burette, dilute acid, about $N/10$, is added, until the liquid is red.

To the clear liquid add Rochelle salts, approximately one Gm. for each Gm. alkaloid present, and while the liquid is still hot, more of the dilute acid is added until the liquid is a decided red, not a pink. Allow to stand in a cool place at least two hours, or better over night. This does not precipitate all the quinine, but should reduce the ratio of quinine to strychnine. At this stage there is a possibility of some strychnine being carried down with the quinine, if not acid enough.

The tartrate precipitate and solution is filtered by suction as rapidly as possible, and washed from the dish onto the filter, using about 50 cc. of water in all, then dropwise the edge of filter is washed with about 10 cc. more of water. The filtrate from this tartrate with its washings are placed in a large enough separator, and the alkaloids in the solutions extracted with chloroform and ammonia, the chloroform evaporated or distilled off, the residue of alkaloids with its small amount of solvent dissolved with sufficient excess of dilute hydrochloric acid; this acid solution with its washings placed in a dish, and evaporated on a water-bath. When nearly dry, a fair amount of free hydrochloric acid should be given off. Evaporate to dryness, mixing with a stirring rod, if need be, then add a little water and evaporate again to dryness. This should drive off all excess of hydrochloric acid. It should not be kept on the water-bath longer than necessary, and if possible, have the water-bath a little below boiling.

Ammonia fumes must be kept away from the acid solution of the alkaloids while evaporating to dryness.

The dry residue in the dish is taken up with a small amount of water, washed into a 100-cc. flask or cylinder, brought up to mark, mixed and 50 cc. of this transferred to a titrating vessel; a wide mouth bottle with a clear bottom is very good to see the color changes. A few drops of methyl red indicator are added and then the liquid is titrated to a pure yellow with $N/50$ sodium hydrate, and cc. used noted. A white surface placed under the bottle shows the color changes very well.

The other 50 cc. of liquid is transferred to another titrating vessel, then 50 cc. of 95% neutral alcohol added, then some phenolphthalein indicator, and titrated with the $N/50$ soda to a faint pink which remains so for at least one-fourth minute, and number of cc. noted. The error by measuring this way is practically negligible for this case.

Then make a blank test, using 50 cc. of same alcohol with 50 cc. of water and phenolphthalein indicator and note the number of cc. of $N/50$ required to obtain same slight pink.

From the number of cc. of second titration subtract the number of cc. for the blank test, then from this subtract twice the number of cc. used in the first titration, and this difference multiplied by two, should give the amount of $N/50$ for the strychnine.

To reiterate, it is important that the hot acid solution, wherein the tartrate is precipitated, is made sufficiently acid again while hot after the addition of the Rochelle salt, but not acid enough so as to dissolve too much of the precipitate. If not enough free acid present, some strychnine, or many other alkaloids, if present, will be carried down with the tartrate, about 0.020 Gm. more or less of strychnine when about 2 Gm. of quinine is precipitated, the amount of liquid not having such a large influence.

ASSAY METHOD FOR THE DETERMINATION OF AN ALKALOID OR TOTAL ALKALOIDS IN COATED OR UNCOATED TABLETS.*

BY LESTER C. DICK.

Coated tablets, except sugar-coated, white, are placed in a beaker and the interfering color removed by washing with a solvent.

The tablets are dried at 100° C. and fifty or more are weighed, the average weight noted and the tablets reduced to a fine powder.

Uncoated tablets are directly weighed and reduced to a fine powder. An aliquot part is taken—in either case representing about two grains of alkaloidal salt. The powder is transferred to a Florence flask of 300 cc. capacity, fitted with a tight stopper.

Ammonium hydroxide or sodium hydroxide T. S. is now added in quantity sufficient to liberate the alkaloid. A number of buckshot, depending upon the quantity of powder taken, are now added in amount necessary to subdivide the moist mass. Exactly 100 cc. of chloroform is added, the flask stoppered and rotated, thus coating the sides of flask with the moist powder.

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* Scientific Section, A. PH. A., Toronto meeting, 1932. No discussion.

Rotation of the flask at frequent intervals causes the buckshot to coat and recoat the sides of the flask with a thin layer of the moist powder, insuring complete extraction of the alkaloid or alkaloids by the chloroform. After carrying out the above procedure for several hours the chloroform is poured through a small filter paper and an aliquot part of 50 cc. collected.

The aliquot portion referred to is carefully transferred to a separatory funnel and extracted with dilute acid. The dilute acid is in turn made alkaline with ammonium or sodium hydroxide T. S. and extracted with chloroform. A test should be made in each case to insure complete extraction of the alkaloid. The final chloroform extractive is evaporated and the alkaloids determined either volumetrically or gravimetrically.

The weight of the alkaloid obtained multiplied by 2 gives the amount in the total sample used. The weight of the total sample used divided by the predetermined weight of one tablet gives the number of tablets containing the determined quantity of alkaloid or alkaloidal salt.

In many cases tablets containing no other chloroform-soluble material, the 50-cc. aliquot portion can be evaporated to dryness, the residue dissolved in 10 cc. of neutral dilute alcohol and directly titrated, using methyl red as the indicator, diluting the alcoholic solution to 100 cc. with distilled water after sufficient volumetric acid has been added to give a pink tint.

The following results were obtained in coated tablets by this method:

Tablet.	Theoretical Strychnine Sulphate Content.	Results.	Percentage.
A—	0.00216 Gm.	0.002088 Gm.	96.71
B—	0.00162 Gm.	0.001649 Gm.	101.25
C—	0.00216 Gm.	0.0021297 Gm.	98.60
D—	0.00108 Gm.	0.001025 Gm.	95.82
E—	0.00108 Gm.	0.001025 Gm.	95.82
F—	0.00108 Gm.	0.001022 Gm.	94.59

The thoretical Strychinine Sulphate contents above were obtained from the labeled quantity and do not make allowance for possible errors in manufacture although this in each instance was done under rigid control.

Any other solvent where chloroform is not indicated may be used with equally consistent results.

CONTROL LABORATORY,
G. S. STODDARD & CO., INC.

SUGGESTED ASSAYS FOR SOME N. F. PREPARATIONS.*

STRONG RESORCINOL PASTE. MILD RESORCINOL PASTE.

BY WILLIAM B. BAKER.

The efficacy of the official resorcinol pastes as therapeutic agents is due mainly to the resorcinol and zinc oxide which they contain. It is, therefore, essential that standards be adopted fixing definitely the content limits of these ingredients, and that practical methods be developed for the quantitative determination of the

* From the laboratory of A. G. DuMez, Professor of Pharmacy, School of Pharmacy, University of Maryland.

same. With this object in view, the effort was made to adapt the methods of the U. S. P. X for the assay of resorcinol and zinc oxide, respectively, to the quantitative determination of these substances in the resorcinol pastes in question. The results obtained proved to be entirely satisfactory. These results, together with detailed descriptions of procedures, follow.

EXPERIMENTAL PART.

Preparation of Samples.—Samples of Strong Resorcinol Paste and Mild Resorcinol Paste were carefully prepared according to the directions given in the National Formulary V, assayed samples of resorcinol and zinc oxide being used in each case. Assay results showing the purity of resorcinol and zinc oxide follow:

Assay of Resorcinol and Zinc Oxide for Purity.—The methods prescribed by the United States Pharmacopœia X were followed for the assay of these materials for purity.

TABLE I.—RESULTS OF ASSAY OF RESORCINOL FOR PURITY (U. S. P. X METHOD).

Wt. of Sample in Gm.	Cc. of 0.1 *N* Br_2 Added.	Cc. of 0.1 *N* $Na_2S_2O_3$ Required.	Cc. of 0.1 *N* Br_2 Consumed.	Per Cent Purity of Resorcinol.
1.67	53.92	9.31+	44.60+	98.026
1.60	53.92	11.21+	42.71−	97.96
1.583	53.92	11.62−	42.30+	98.074
1.595	53.92	11.36+	42.56−	97.923
			Average	97.99

TABLE II.—RESULTS OF ASSAY OF ZINC OXIDE FOR PURITY (U. S. P. X METHOD).

Wt. of Sample in Gm.	Cc. of *N* H_2SO_4 Added.	Cc. of *N* NaOH Required.	Cc. of Excess Acid Consumed.	Per Cent Purity of Zinc Oxide.
1.6511	54.435	15.09+	39.33+	96.94
1.5083	54.435	18.49+	35.94+	96.96
1.7806	54.435	12.05+	42.38−	96.84
1.6478	54.435	15.10−	39.33+	97.13
			Average	96.97

Assay of Strong Resorcinol Paste. (1) *Determination of Resorcinol.*

Reagents.—1. 0.1 *N* Bromine Water (Koppeschaar's Solution, U. S. P. X).
2. Hydrochloric Acid, U. S. P. X.
3. Potassium Iodide T.S.
4. 0.1 *N* Sodium Thiosulphate Solution.
5. Starch T.S.

Procedure.—Place 1 Gm. of the paste, accurately weighed, in a 250-cc. flask, add 40 cc. of hot water, stopper the flask tightly and shake it vigorously. Decant the supernatant liquid onto a wetted filter and collect the filtrate in a 100-cc. volumetric flask. Repeat the shaking out process with two 15-cc. portions of hot water, decanting after each extraction. Finally, rinse the contents of the flask onto the filter and wash with sufficient hot water to make 100 cc. of filtrate. Carefully preserve the filter and its contents for the determination of zinc oxide as directed below under "Assay for zinc oxide." Transfer 40 cc. of the filtrate, representing two-fifths of the weight of the paste taken, to a 500-cc. glass-stoppered flask having a long, narrow neck, add 50 cc. of tenth-normal bromine, dilute with 50 cc. of distilled water, add 5 cc. of hydrochloric acid, and at once stopper the

flask. Shake the mixture, allow it to stand for one minute, dilute it with 20 cc. of distilled water, add 5 cc. of potassium iodide T.S., allow it to stand for five minutes, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch test solution as indicator. Each cc. of tenth-normal bromine corresponds to 0.001835 Gm. of $C_6H_4(OH)_2$.

TABLE III.—RESULTS OF ASSAY FOR RESORCINOL CONTENT.

Wt. of Sample in Gm.	Cc. of 0.1 *N* Br_2 Added.	Cc. of 0.1 *N* $Na_2S_2O_3$ Required.	Cc. of 0.1 *N* Br_2 Consumed.	Gm. of $C_6H_4(OH)_2$ Found per 100 Gm. Strong Resorcinol Paste.
1.0902	53.405	6.83+	46.56+	19.57
1.0446	53.405	9.11+	44.28+	19.47
1.1825	53.405	3.30−	50.10−	19.43
1.0822	53.405	7.86−	45.54−	19.53
			Average	19.50

Calculated percentage of resorcinol in sample (20 × 97.99) = 19.598
Average percentage of resorcinol found in sample = 19.50
Difference = 00.098

Percentage error (00.098 ÷ 19.598) × 100 = 0.505

(2) *Determination of Zinc Oxide.*

Reagents.—1. Normal Sulphuric Acid.
2. Normal Sodium Hydroxide Solution.
3. Methyl Orange T.S.

Procedure.—Place the filter used in the preceding assay, together with its contents, into a small porcelain crucible and ignite to get rid of the liquid petrolatum and any starch which may be present. Digest the residue remaining in the crucible after ignition with 50 cc. of normal sulphuric acid until solution is complete. Then titrate the excess of sulphuric acid with normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.04069 Gm. of ZnO.

TABLE IV.—RESULTS OF ASSAY FOR ZINC OXIDE CONTENT.

Wt. of Sample in Gm.	Cc. of *N* H_2SO_4 Taken.	Cc. of *N* NaOH Used.	Cc. of Excess Acid.	Gm. of ZnO per 100 Gm. Strong Resorcinol Paste.
1.0902	48.385	43.08−	5.30−	19.79
1.0446	48.385	43.31+	5.06+	19.73
1.1825	48.385	42.61+	5.76+	19.85
1.0822	48.385	43.19+	5.18+	19.49
			Average	19.715

Average percentage of zinc oxide found in sample = 19.715
Calculated percentage of zinc oxide in sample (20 × 96.97) = 19.394
Difference = 00.321

Percentage error (00.321 ÷ 19.394) × 100 = 1.65

DISCUSSION.

The methods for the quantitative determination of resorcinol and zinc oxide described above, as previously stated, are essentially those given in the U. S. P. X for the determination of the purity of these substances, and no great difficulty was experienced in carrying them out after the substances were isolated. The isolation of the substances, likewise, presented little difficulty, as the resorcinol is

completely removed from the paste by shaking out with hot water and passing the washings through a filter. The zinc oxide and other insoluble matter composing the base of the paste are retained by the filter. After ignition, the zinc oxide content can readily be determined by titration.

The above methods were also applied to the quantitative determination of resorcinol and zinc oxide in Mild Resorcinol Paste and they were found to be equally as well suited to the assay of this preparation as to the assay of the strong paste.

Since the methods described above are comparatively simple, give accurate and concordant results, it is recommended that they be adopted for admission to the National Formulary, and that the following standards be prescribed for the resorcinol pastes contained therein:

Suggested Standards: Strong Resorcinol Paste.—One hundred grams of Strong Resorcinol Paste contain not less than 19 Gm. and not more than 21 Gm. of $C_6H_4(OH)_2$, and not less than 19 Gm. and not more than 21 Gm. of ZnO.

Mild Resorcinol Paste.—One hundred grams of Mild Resorcinol Paste contain not less than 9.5 Gm. and not more than 10.5 Gm. of $C_6H_4(OH)_2$, and not less than 24 Gm. and not more than 26 Gm. of ZnO.

STUDIES ON THE PREPARATION, TOXICITY AND ABSORPTION OF BISMUTH COMPOUNDS. II. BISMUTH SALTS OF ALIPHATIC HYDROXY ACIDS.*

BY W. M. LAUTER, A. E. JURIST AND W. G. CHRISTIANSEN.

A great deal of work has been done with one acid of this series, namely, tartaric acid. The sodium and potassium salts of this acid in combination with bismuth have been used extensively in the treatment of syphilis both in aqueous solution and in oil suspension. Also a number of investigators have studied both the preparation of these compounds and their absorption, excretion and toxicity in animals.

The composition of bismuth tartrates and their preparation by different methods have been described by Rosenheim and Vogelsang (1), Cowley (2), Bauer (3), Maschman (4), Warren (5), Corfield and Adams (6, 7), Barthe (8), Fabregue (9), Picon (10), Godfrin (11), Von Oettingen and Ishikawa (12), Volmer (13), Hehner and Likiernik (14), Kober (15), Von Oettingen, Sollmann and Schweid (16), and Yoe and Mote (17). The toxicity, absorption and excretion of these compounds have been discussed by Ducrey (18), Pautrier (19), Didry (20), Pomaret and Didry (21), Raiziss and Brown (22), Raiziss and Severac (23), Giemsa (24), Giemsa and Weise (25), Lomholt (26), and Pacella (27). Also Browning, Cohen, Gulbransen, Phillis and Snodgrass (28) studied the comparative therapeutic action of the bismuth salts of several organic hydroxy acids including tartaric acid, gluconic acid, mannonic acid and others. An investigation of the effect of different solvent media on the absorption of and local reactions produced by bismuth tartrates in dogs was reported by Jurist and Christiansen (29).

The purpose of this investigation was to compare the toxicity and absorption of bismuth tartrates in aqueous solution and in oil suspension with bismuth tartrates and bismuth mucates combined with mannite, and with bismuth mucates

* Scientific Section, A. PH. A., Toronto meeting, 1932.

in aqueous solution. In these studies the same method was used in studying the absorption and toxicity as that used in the investigation of the bismuth salts of the fatty acids. The time allowed for absorption was extended to 60 days in this instance as compared to the 27- to 35-day period used in studying the fatty acids.

The preparations were injected intramuscularly into albino rats either in water solution or oil suspension. The per cent absorption was determined by killing the animal and estimating by analysis any bismuth remaining unabsorbed at the site of injection. The toxicity was determined as in the study of the fatty acid compounds from the growth curves of the albino rats. The following table contains the results obtained.

TABLE I.

Compound Injected.	Nature of Medium for Injection.	Dosage Mg. Bi/Cc.	Per Cent Absorbed.	Approximate Maximum Tolerated Dose Mg./Kg. Body Weight.
Sodium Tri-Bismuth Tartrate	Water	35	100	600
Sodium Tri-Bismuth Tartrate	Water	35	100	600
Sodium Tri-Bismuth Tartrate	10% Aqueous glucose	50	96	500
Sodium Tri-Bismuth Tartrate	10% Aqueous glucose	50	87	500
Sodium Tri-Bismuth Tartrate	Olive oil	35	...	600
Sodium Tri-Bismuth Tartrate	Olive oil	35	...	600
Sodium Potassium Bismuth Tartrate	10% Aqueous glucose	35	100	50
Potassium Tri-Bismuth Tartrate	Olive oil	33.5	37–81.5	400
Sodium Bismuth Tartro-Mannitan	Water	50	100	250
Sodium Bismuth Tartro-Mannitan	Olive oil	50	90	...
Sodium Bismuth Mucate	10% Aqueous glucose	50	90	300
Sodium Bismuth Muco-Mannitan	10% Aqueous glucose	50	90	400

These results demonstrate clearly the fact that water-soluble bismuth preparations are much more readily absorbed than the water-insoluble compounds; absorption of insoluble compounds is discussed in Paper I of this series. Even when administered in olive oil suspension there is a very high percentage of absorption, since this exceeds 90% in all but two instances in the series of twelve tests made. The only experiments giving wide variations in absorption were those with potassium tartrate in olive oil. The average absorption excluding the latter material which gave irregular results was 95%. With water solutions and 10% aqueous glucose solutions the absorption was nearly complete in 72 hours. A more extended period was required for the absorption of the olive oil suspensions.

The toxicity of the tartrates was a little less than that of the mucates and it was also less than that of the complex compounds with mannite. The single exception was sodium potassium bismuth tartrate. This substance was far more toxic than the other tartrates although there was little difference in the completeness and rapidity with which they were absorbed. However, with this single exception, all of the bismuth derivatives of tartaric and mucic acids tested were relatively low in toxicity.

The completeness and rapidity with which these water-soluble compounds are absorbed and their low toxicity indicate that they are more satisfactory therapeutic

agents than the bismuth salts of the fatty acids. However, the objection to these compounds is their tendency to produce local reactions of some severity at the site of injection as was pointed out in a previous publication (29).

The biological tests on these compounds were carried out in the Biological Laboratories of E. R. Squibb and Sons, New Brunswick, N. J.

EXPERIMENTAL PART.

Preparation of Sodium Bismuth Mucate.—Five and six-tenths grams of mucic acid were dissolved in 600 cc. of water and 155 cc. of a bismuth subnitrate solution, prepared by dissolving 150 Gm. of bismuth subnitrate in 150 cc. of concentrated nitric acid (sp. gr. 1.41) made up to one liter with water, are mixed and a white precipitate is formed. This was collected on a Buchner funnel and washed with water, alcohol and ether; 10 Gm. of this solid were suspended in 100 cc. of water and dissolved by means of sodium hydroxide. An equal volume of 95% alcohol was added and a white precipitate formed. This was collected on a Buchner funnel, washed with alcohol and ether and dried.

Calculated for $CO_2Na—CHOBiO—CHOBiO—(CHOH)_2—CO_2Na$: Na—6.55%, Bi—59.6%. Found: Na—6.1%, Bi—60.1%.

Preparation of Sodium Bismuth Muco-Mannitan.—Thirty-seven and one-tenth grams of sodium bismuth mucate and 30 Gm. of mannite were dissolved in about 200 cc. of water and neutralized with 20% sodium hydroxide. After warming for $^1/_2$ hour on the steam-bath the solution was cooled and twice the volume of acetone was added. A brown syrup precipitated. The supernatant liquor was decanted and the residue was washed several times with acetone, and then with absolute alcohol and ether. A finely divided white powder was obtained.

Calculated for $CO_2Na—HCOBiO—(C_6H_{10}O_4)_2—(CHONa)_2—CHOBiO—CO_2Na—(C_6H_{10}O_4)$: Bi—31.5%; Na—6.9%; acetyl number, 20.0. Found: Bi—30.09%; Na—5.87%; acetyl number, 19.6.

Preparation of Sodium Tribismuth Tartrate.—Eighty-six cc. of a solution, prepared by dissolving 150 Gm. of bismuth subnitrate in 150 cc. of concentrated nitric acid and then diluted to one liter with water were run into 200 cc. of sodium hydroxide solution containing 8 Gm. of sodium hydroxide. The suspension was adjusted with concentrated nitric acid until weakly alkaline to litmus. The bismuth hydroxide so obtained was then collected on a Buchner funnel and washed with water. The freshly prepared, wet bismuth hydroxide was then suspended in 50 cc. of water, and 40 cc. of a solution containing 8 Gm. of tartaric acid and 4.3 Gm. of sodium hydroxide were added. The mixture was heated on the steam-bath for two hours and then cooled. The small amount of insoluble matter was removed by filtration. The clear filtrate was then treated with an equal volume of 50% alcohol. A white precipitate gradually separated. The solid was collected on a Buchner funnel, washed with 95% alcohol and ether. The dry white powder was readily water soluble.

Calculated for $C_4H_3O_9Bi_3Na$: Bi—74.29%. Found: Bi—72.33%.

Preparation of Potassium Tribismuth Tartrate.—The method used was the same as that used for the sodium salt except that potassium hydroxide was used instead of sodium hydroxide.

Preparation of Sodium Bismuth Tartro-Mannitan.—Eighty-six cc. of the same bismuth nitrate solution used above were treated with 40 cc. of an aqueous solution of 8 Gm. of tartaric acid while stirring at room temperature. After standing for 10 minutes 21.8 Gm. of sodium bicarbonate in 250 cc. of water were added. Vigorous effervescence occurred with the formation of a white precipitate. The mixture was heated for 30 minutes at 85° C., then the mixture was allowed to stand over night. The white solid was collected on a Buchner funnel and washed with water. The product was insoluble in water but soluble in aqueous sodium hydroxide, 10 Gm. of this solid, 10 Gm. of mannite and 150 cc. of water were treated, warm with dilute aqueous sodium hydroxide until a clear solution resulted. This solution was treated with two volumes of acetone precipitating a yellow oil. After the supernatant liquor was poured off, the oil was further washed successively with acetone and ether and converted into a solid by treatment with absolute alcohol. The solid so obtained was washed with absolute alcohol and ether. The solid was water soluble and contained 30.99% of bismuth, 6.68% of sodium and 35.92% of mannite calculated from the acetyl number.

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STUDIES ON THE PREPARATION, TOXICITY AND ABSORPTION OF BISMUTH COMPOUNDS. III. IODOBISMUTHATES OF ALKALOIDS.*

BY W. M. LAUTER, A. E. JURIST AND W. G. CHRISTIANSEN.

The alkaloids in combination with bismuth iodide have been known for a considerable time since Draggendorf (1) in 1866 utilized the bismuth iodide and hydriodic acid double salts to precipitate the alkaloids from acid solution. Since that time a number of investigators have studied the chemical composition and analysis of these substances including Pozzi-Escot (2), Aubry and Demelin (3), Azoulay (4), Francois and Blanc (5), (6), Bardet (7), Francois and Seguin (8), Isnard (9, 10), Rabak (11), and Ewe (12). More recently the iodobismuthates of quinine and emetine have received extensive use in the treatment of syphilis. The excretion, absorption and toxicity of these compounds have been studied by Lomholt (13), Jeanselme (14), and Lacapere, Restoux and Bugeard (15).

In this investigation the iodobismuthates of quinine and emetine were prepared by the methods already available and also the iodobismuthate of procaine was prepared.

These compounds are all insoluble in water and it was necessary, therefore, to inject them in oil suspension. As in the case of the fatty acid salts of bismuth and the bismuth tartrates, etc., the suspensions were injected intramuscularly into albino rats. The absorption was determined by estimating quantitatively the unabsorbed bismuth at the site of injection while the toxicity was estimated from the growth curves of the animals. The results obtained in these studies are given in the following table.

TABLE I.

Compound Injected.	Nature of Medium for Injection.	Bismuth Conc. Mg. Bi/Cc.	Approx. Maximum Tolerated Mg./Kg. Body Wt.	% Absorption.
Iosobismuthate of Quinine	Olive oil	20	Less than 400	50–60%
Iodobismuthate of Emetine	Olive oil	15	Less than 15	Slow
Iodobismuthate of Procaine	Olive oil	30	150	100%

These substances differ considerably in toxicity. The least toxic, the iodobismuthate of quinine, is, however, only 50 to 60% absorbed. This is not satisfactory from the therapeutic standpoint when such a result is compared to the rapidly and completely absorbed water-soluble compounds. The results obtained with the iodobismuthate of emetine were entirely unsatisfactory. In addition to being very slowly absorbed it was extremely toxic. Its high toxicity of less than 15 mg. per Kg. of body weight makes it unsuitable for therapeutic purposes. The iodobismuthate of procaine, a new compound, appears to be the best of this type of substance, although procaine cannot be classed as an alkaloid. The complete absorption of this compound coupled with the fact that it is not very toxic may be taken as an indication that it might be a satisfactory therapeutic agent. As a class, however, the iodobismuthates of the alkaloids in the form tested are not entirely satisfactory therapeutic agents because of their slow and incomplete absorption.

* Scientific Section, A. PH. A., Toronto meeting, 1932.

EXPERIMENTAL PART.

Preparation of the Iodobismuthate of Quinine.—One gram of quinine hydrochloride was dissolved in 100 cc. of water. This was mixed with a solution of 1 Gm. of bismuth subnitrate in 4.7 Gm. of potassium iodide and 5 cc. of acetic acid in 100 cc. of water. The red precipitate which immediately formed was collected on a Buchner funnel and washed with water. This was then dried *in vacuo* over phosphoric anhydride.

Calculated for $C_{20}H_{24}N_2O_2$, 2HI, $2BiI_3$: Bi—23.7%; $C_{20}H_{24}N_2O_2$—18.7%. Found: Bi—23.7%; $C_{20}H_{24}N_2O_2$—19.2%.

Preparation of the Iodobismuthate of Emetine.—The same method as that used in the preparation of the quinine derivative was used here. The compound is a red powder.

Calculated for $C_{29}H_{40}O_4N_2$, HI, BiI_3: Bi—17.4%; $C_{29}H_{24}O_4N_2$—40.2%. Found: Bi—14.1%; $C_{29}H_{40}O_4N_2$—31.5%.

Preparation of the Iodobismuthate of Procaine.—One gram of bismuth subnitrate was dissolved in 5 cc. of hydrochloric acid and mixed with 4.7 Gm. of potassium iodide in 100 cc. of water. This was mixed with 1 Gm. of procaine hydrochloride dissolved in 100 cc. of water. The deep red precipitate which formed immediately was collected on a Buchner funnel, washed with water, and dried *in vacuo* over phosphoric anhydride.

Calculated for $C_{13}H_{20}N_2O_2$, 2HI, $2BiI_3$: Bi—12.3%; $C_{13}H_{20}N_2O_2$—22.89%. Found: Bi—14.5%; $C_{13}H_{20}N_2O_2$—21.70%.

The Biological tests on these compounds were carried out in the Biological Laboratories of E. R. Squibb and Sons, New Brunswick, N. J.

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It may be that some day it will be said, "1932 was a hard year, but without it we would not have had the new tonic and cleansing resolves which will help us get out of the trough of the sea in which our ship was in danger of foundering."

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THE MELTING POINT OF ACETYLSALICYLIC ACID.*

PUBLISHED BY PERMISSION OF THE CHAIRMAN OF THE COMMITTEE OF REVISION, U. S. P. XI.

BY GEORGE D. BEAL[1] AND CHESTER R. SZALKOWSKI.[2]

There has been some dissatisfaction expressed regarding the method of U. S. P. X for the determination of the melting point of acetylsalicylic acid. The method of the U. S. P. reads as follows:

"The melting point of Acetylsalicylic Acid, when finely powdered, and determined in a bath previously heated to 120° C., is not below 132° C."

According to D. A. B. VI, the determination is made as follows:

"For determination of the melting point the bath is brought to about 125° C. before introducing the melting point tube, and then heated with a greater flame, so that the temperature mounts at the rate of 1° every ten to fifteen seconds."

Both sets of directions evidently recognize the tendency of this acid to decompose while being heated, the products of decomposition forming an eutectic with the unchanged acid, thus depressing its melting point beyond the true value.

The U. S. P. X regards 132° C. as the melting point, the German Pharmacopœia 135° C., the British Pharmacopœia 133°–135° C. [135°–138° in the 1932 revision], the Japanese Pharmacopœia 135° C., and New and Non-Official Remedies 128°–133° C.

Attention has already been called to this by Carswell,[3] Dahm[4] and Putnam.[5] Carswell concludes that the melting point of the acid is dependent upon the size of the particles in the tube; that fine grinding is essential, 200 mesh being recommended; and that variations in melting point after crystallization from various solvents are caused by differences in the physical structure of the crystals, since fine grinding gives uniform values.

Dahm recommends a special form of apparatus, including a stirrer, and suggests an allowable range of 133°–135° C., which seems very wide.

Putnam recommends an initial bath temperature of 120° C., then heating the bath so that the temperature rise is 3° C. per minute, introducing the melting-point tube at 130° C. and continuing heating until the sample melts. The acid in melting passes through three stages; (*a*) moist stage, (*b*) formation of first globule, (*c*) complete liquefaction with definite meniscus. The second stage was taken as the true melting point. A value of 133.5 is therefore recommended as the true melting point.

In the authors' work sulphuric acid was used as the bath, in a round-bottomed Pyrex tube of 45 mm. internal diameter and 10 cm. long. A stirrer was made of a glass rod bent into a ring at a right angle to the stem, the handle then being bent back upon itself at two right angles. The thermometer had a range of 93°–165° C., was graduated in 0.2°, and had been calibrated at the U. S. Bureau of Standards. The bulb of the thermometer was placed at 2–3 cm. from the bottom of the bath,

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* Section on Practical Pharmacy and Dispensing, A. PH. A., Toronto meeting, 1932.

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[2] Assistant, Department of Research in Pure Chemistry, Mellon Institute.

[3] JOUR. A. PH. A., 16 (1927), 306.

[4] *Ind. Eng. Chem.*, 11 (1919), 29. [5] *Ibid.*, 16 (1924), 778.

and submerged to the 136° mark, obviating an emergent stem correction. The capillary melting-point tubes varied in internal diameter from 0.8 to 1.0 mm., with walls not over 0.3 mm. in thickness.

The acetylsalicylic acid was powdered in a glass mortar and thoroughly dried in a desiccator over sulphuric acid. Separate portions were ground to 100, 150 and 200 mesh. The powder was charged into the tube to a height of 2.5 to 3 cm., and was lightly packed by drawing the corner of a file across the tube and then gently tapping the tube on a hard surface. The lower end of the tube was sealed in all instances, and some comparisons were made by sealing the top end as well.

The temperature at which the substance begins to collapse against the wall of the tube was recorded as the beginning of melting, while the temperature at which the mass became clear throughout was recorded as the actual melting point.

Four samples of acetylsalicylic acid, furnished by manufacturers, were used in these measurements. An initial bath temperature of 120° C. with increments of 3° and 5° per minute were used in the determinations recorded in Table I, and of 130° C. with the same increments in Table II.

TABLE I.—EFFECT OF FINENESS OF POWDER AND RATE OF HEATING. INITIAL TEMPERATURE OF BATH, 120° C.

Average of 8 Determinations.

Sample.	Fineness.	Heated 3° per Minute. Incipient Fusion.	M. P.	Heated 5° per Minute. Incipient Fusion.	M. P.
A	100	130.0	132.7	131.0	133.6
B	100	130.6	133.1	131.0	133.6
C	100	130.0	132.5	132.0	133.5
D	100	130.0	132.2	131.7	133.1
Average	100	130.15	132.6	131.4	133.45
A	150	130.0	132.5	130.0	133.5
B	150	130.2	132.5	131.0	133.6
C	150	130.6	132.5	131.3	133.65
D	150	129.0	132.3	130.0	133.5
Average	150	129.95	132.45	130.57	133.56
A	200	130.0	132.1	131.2	133.5
B	200	130.0	132.25	131.0	133.4
C	200	130.2	132.45	132.0	133.9
D	200	129.5	132.0	131.2	133.3
Average	200	129.9	132.2	131.35	133.5
		Tube sealed at both ends			
A	200	129.2	130.6		
B	200	129.4	130.9		
C	200	129.2	130.9		
D	200	129.0	130.7		
Average	200	129.2	130.73		

TABLE II.—EFFECT OF FINENESS OF POWDER AND RATE OF HEATING. INITIAL TEMPERATURE OF BATH, 130° C.

Average of 8 Determinations.

Sample.	Fineness.	Heated at 3° per Minute. Incipient Fusion.	M. P.	Heated 5° per Minute. Incipient Fusion.	M. P.
A	100	133.0	135.4	133.0	135.6
B	100	133.0	135.6	133.0	135.6
C	100	133.0	135.4	133.6	135.8
D	100	132.4	135.4	133.1	135.7
Average	100	132.85	135.45	133.2	135.7

TABLE II.—EFFECT OF FINENESS OF POWDER AND RATE OF HEATING. (*Continued.*)

Sample.	Fineness	Heated at 3° per Minute. Incipient Fusion.	M. P.	Heated 5° per Minute. Incipient Fusion.	M. P.
A	150	131.7	135.1	132.4	135.3
B	150	132.2	135.3	133.0	135.3
C	150	133.0	135.1	133.0	135.4
D	150	132.0	134.8	132.5	135.3
Average	150	132.2	135.1	132.7	135.3
A	200	132.6	135.45	133.0	135.6
B	200	132.3	135.2	133.0	135.9
C	200	133.0	135.25	132.9	135.8
D	200	131.7	134.6	132.1	135.2
Average	200	132.4	135.1	132.75	135.6

A trial was made of Dahm's method. The same test-tube was used as a container for the bath, which in this case was of glycerine. A motor-driven glass stirrer was used. All other conditions were as previously described, the acid being ground to 200 mesh and dried over sulphuric acid over night.

TABLE III.—DAHM'S METHOD.

Sample.	Fineness.	Initial Temperature.	Rate of Heating ° per Minute.	M. P.	Sealed Tube, M. P.
A	200	130°	1	133.4	.....
A	200	130°	3	135.7	133.7
B	200	130°	1	133.2	.....
B	200	130°	3	135.7	134.8
C	200	130°	1	133.3	.....
C	200	130°	3	135.8	134.6
D	200	130°	1	133.0	.....
D	200	130°	3	135.2	134.5

Another series of determinations was carried out to determine the time required for complete fusion when the temperature of the bath was held at any given point. Glycerine was used for the bath. The samples were ground to 200 mesh and dried over night over sulphuric acid. All other details were the same except that the sample was introduced when the bath had reached the desired temperature and was then held at that point until melting had occurred.

TABLE IV.—NO. OF SECONDS REQUIRED FOR COMPLETE FUSION AT GIVEN TEMPERATURES.

Samples.	133.8°–134.4°.	134.8°–135.4°.	135.8°–136.4°.	136.8°–137.2°.
A	...	79 sec.	59 sec.	50 sec.
B	110 sec.	81 sec.	65 sec.	53 sec.
C	...	80 sec.	62 sec.	53 sec.
D	...	76 sec.	64 sec.	52 sec.

Samples.	137.8°–138.2°.	138.8°–139.4°.	145°–146°.
A	39 sec.	25 sec.	10 sec.
B	36 sec.	28 sec.	12 sec.
C	39 sec.	31 sec.	11 sec.
D	33 sec.	26 sec.	11 sec.

The melting points of the four samples of acetylsalicylic acid were finally determined by means of the copper bar apparatus of Dennis and Shelton.[1] Melt-

[1] *J. Am. Chem. Soc.*, 52 (1930), 3128.

ing points were determined for both the crystalline samples and the samples when powdered to 200 mesh. All samples were dried in the desiccator according to our usual procedure. There was a slight reaction with the bar, evidenced by the appearance of a slight green color.

TABLE V.—MELTING POINT OF ACETYLSALICYLIC ACID BY DENNIS AND SHELTON COPPER BAR.

Samples.	Fineness.	Actual Observations.	Average.
A	Crystals	142.3, 142, 141.9, 142, 141.6, 141.8	141.6
A	200	142, 141.8, 142.2, 142, 142	142.0
B	Crystals	142, 142.2, 141.5, 142.5, 142	142.0
B	200	142, 141.6, 141.9, 142.2, 141.8, 142	141.9
C	Crystals	141.8, 142, 142.2, 141.6, 142.4	141.96
C	200	142, 141.7, 142, 141.8, 141.5	141.8
D	Crystals	141.5, 141.8, 142, 141.4, 141.8, 141.6	141.7
D	200	141.5, 141.2, 141.8, 141.5, 142	141.6

It is very evident from these experiments that acetylsalicylic acid melts with decomposition, and that a part of this decomposition takes place before the acid has melted, resulting in a lowering of the melting point of the sample under observation. To test this further, melting-point tubes containing the various samples were allowed to solidify for 24 hours after the first melting, and were then subjected to a redetermination of the melting point, using exactly the same procedure as followed in the original determination.

TABLE VI.—DEPRESSION OF MELTING POINT OF ACETYLSALICYLIC ACID UPON REMELTING.

		Initial Bath Temp. 120° C. Heating Rate 3° per Min.		Initial Bath Temp. 130° C. Heating Rate 3° per Min.	
Sample.	Fineness.	1st M. P.	2nd M. P.	1st M. P.	2nd M. P.
A	200	132.1	129.7	135.4	133.5
B	200	132.2	130.0	135.2	134.1
C	200	132.4	130.4	135.2	134.1
D	200	132.0	129.1	134.6	133.2

To determine the effect of continued heat on the melting point of the acid, Samples B and C, prepared as usual, were placed in tubes in a bath heated to 125° C., and held at a temperature between 124° and 125° C. until the samples had melted. The experiment was also carried out at a temperature of 120° C. The tubes were then cooled over night and the melting point redetermined by the method we are recommending, *viz.*, an initial bath temperature of 130° C. and a heating increment of 3° per minute. The results were as follows:

TABLE VII.—TIME REQUIRED TO MELT ACETYLSALICYLIC ACID AT FIXED TEMPERATURES.

Sample.	Fineness.	Bath Temperature.	Minutes to Melt.	M. P. When Remelted by Standard Method.
B	200	124–5	21	134.0
B	200	119–20	63	134.2
C	200	124–5	23	130.6
C	200	119–20	69	131.0

It is believed that grinding the acid to a fineness of 200 mesh, and possibly even 150 mesh, causes some slight decomposition, as a slightly lower value is obtained in the routine procedure of Table II than when a 100-mesh powder is used.

Occasionally a slight odor of acetic acid is observed during this heavy grinding. For this reason it is thought that a 100-mesh powder represents the optimum of uniformity to be sought.

As a further test of the possibility of decomposition of acetylsalicylic acid during melting, an analysis, according to the saponification method of the U. S. P. X, was made of the four acids after melting. Melting-point tubes were weighed, charged with the acid, ground to 200 mesh and dried, and weighed again. The melting point was then determined, using an initial bath temperature of 130° C. and a rate of heating of three degrees per minute. After the samples had cooled and solidified, the tubes were freed from adherent bath liquid and weighed a third time. The combined tubes containing each sample were ground in a mortar and the acid dissolved in alcohol. Fifty cc. of half-normal sodium hydroxide were added to the solution and the assay completed according to the official method. The results follow:

TABLE VIII.

Sample.	Fineness.	Purity before Melting.	Purity after Melting.
A	200	99.05	98.40
B	200	99.20	98.27
C	200	99.78	98.40
D	200	99.75	98.80

Samples were also melted as recommended here, with a fine strip of blue litmus paper placed in the top of the tube. The paper became red as the sample melted, showing the evolution of acetic acid, also detectable by its odor.

CONCLUSION.

In the opinion of the authors, the melting point rubric of U. S. P. XI should read as follows:

Acetylsalicylic acid has a melting point not below 135° C. when determined by the following method. Crush the acid to a No. 100 powder and dry in a desiccator over sulphuric acid for twelve hours. Place a column of the powder 2.5 to 3.0 cm. in length in a capillary melting-point tube having an internal diameter of 0.8 to 1.0 mm., sealed at one end. Place the tube in a bath previously heated to 130° C. and continue the heating at the rate of 3° per minute until the acid melts.

PITTSBURGH, PA.,
August 15, 1932.

TINCTURE NUX VOMICA.*

BY V. L. DICKEY AND F. W. NITARDY.

INVESTIGATION OF THE USE OF HYDROCHLORIC ACID AND ACETIC ACID FOR ACIDIFYING THE MENSTRUUM AND THE DETERMINATION OF THE EFFECT OF SLOW AND FAST PERCOLATION.

Experiments were carried out in an attempt to find a more satisfactory method of extracting Nux Vomica. The object was to determine the advantages and disadvantages of menstrua containing hydrochloric acid and acetic acid, respectively,

* Section on Practical Pharmacy and Dispensing, A. PH. A., Toronto meeting, 1932.

and also whether any improvement resulted by slow or rapid extraction. Using 100-Gm. quantities of the same lot of drug in each case, tinctures were prepared with the following variations. The drug used assayed 2.984% alkaloids.

TABLE I.

Experiment.	Menstruum.	Time of Maceration.	Rate of Percolation.
A	1. Alcohol 750 cc.; water 240 cc. Acetic acid 10 cc. 2. Alcohol 3 vol.; water 1 vol.	24 hours	0.5 cc. per min.
B	1. Alcohol 750 cc.; water 245 cc. Hydrochloric acid U. S. P. X 5 cc. 2. Alcohol 3 vol.; water 1 vol.	24 hours	0.5 cc. per min.
C	1. Alcohol 750 cc.; water 242.5 cc. Hydrochloric acid U. S. P. X 7.5 cc. 2. Alcohol 3 vol.; water 1 vol.	24 hours	0.5 cc. per min.
D	(Same menstruum as A)	6 hours	2.0 cc. per min.
E	(Same menstruum as A)	3 hours	4 cc. per min.

On each reserve portion (950 cc.), the assay, acidity and p_H were determined and completeness of extraction was calculated. The results obtained were as follows:

Tincture.	Average of Two Assays.	Degree of Extraction.	Acidity Determination on 10 Cc. of the Tr. Expressed as Cc. N/10 NaOH Required. Phenolphthalein Indicator.	p_H.
A	0.2806 Gm. in 100 cc.	94.03%	7.55 cc.	5.32
B	0.2519 Gm. in 100 cc.	84.42%	5.55 cc.	1.99
C	0.2882 Gm. in 100 cc.	96.58%	8.45 cc.	1.55
D	0.1958 Gm. in 100 cc.	65.62%	7.60 cc.	5.19
E	0.1892 Gm. in 100 cc.	63.4 %	7.49 cc.	5.26

Tinctures A and C being high in assay were adjusted by using a menstruum of alcohol 3 vol.—water 1 vol., making the finished tincture conform to the required U. S. P. standard. Each of the five prepared tinctures was defatted by cooling to 5° C. and filtering. About the same amount of fat appeared to separate from each. Tinctures B, D and E were defatted without adjustment since the alkaloidal content on B was within the U. S. P. range and that of D and E below this range. Samples A and C were re-assayed, the results being as given in the following table:

TABLE II.

Tincture.	Average of Two Assays.	Acidity Determination on 10 Cc. of the Tr. Expressed as Cc. N/10 NaOH Required. Phenolphthalein Indicator.	p_H.
A	0.2475 Gm. per 100 cc.	7.14 cc.	5.45, check 5.43
C	0.2552 Gm. per 100 cc.	7.59 cc.	1.76, check 1.74

Extraction efficiency and completeness seem to depend on adequate maceration and slow percolation combined with a sufficient amount of available acid. The degree to which the acid ionizes seems less important. Tincture A was nearly equal in available acid to tincture C but of much higher p_H. However, extraction was nearly as good and when compared to tincture B which differed from C, only

in the amount of acid used, it would appear that with equal normality in acid present in the menstruum, there would probably be no difference in extraction efficiency between the use of acetic and hydrochloric acids. It also appears that 10 cc. of acetic acid or 7.5 cc. hydrochloric acid represent the minimum amounts per liter of menstruum that should be used and slightly greater amounts may prove still more effective.

Observations were begun on the tinctures two months after preparation, being kept in amber bottles at room temperature in the absence of light.

TABLE III.—SEDIMENTATION OF TINCTURES.

	Age of Tinctures at Observation.		
	2 Months.	3 Months.	7 Months.
Tincture A	−	−	+
Tincture B	+	+	++
Tincture C	+	+	++
Tincture D	−	−	++++
Tincture E	+	+	++

— represents no sediment.
+ represents slight sediment indicating the least.
++++ indicating the largest amount with no great difference between the two extremes.

A close examination was necessary to detect the precipitate in the tinctures as no great quantity was present in any of them. The sediment which does appear may be a trace of fat not removed in the defatting process. The supernatant liquid was clear in all samples.

CONCLUSIONS.

1. Adequate maceration and slow percolation are necessary for complete extraction.

2. Not less than 10 cc. of acetic acid or less than 7.5 cc. of hydrochloric acid per liter of menstruum should be used. Smaller amounts of acid yield less complete extraction.

3. Defatting does not remove alkaloids from the tincture, and aids in avoiding precipitation as the tincture ages.

4. Complete extraction resulting from longer maceration and slower percolation apparently does not lead to greater precipitation on aging. Acetic acid has a slight advantage over hydrochloric acid from standpoint of freedom from sedimentation of the finished tincture.

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Perhaps everyone will admit that if pharmacists magnified their profession to the fullest there would be developed a relatively greater appreciation of it; and, as a result, its opportunities would be developed to a greater extent, and the public could have a better understanding of its worth. There are few industries to which pharmacy has not directly or indirectly contributed; in most of the divisions of science and art, pharmacy has a part and has contributed very largely to the achievements of medicine.

NOTES ON THE PREPARATION OF AROMATIC FLUIDEXTRACT OF CASCARA SAGRADA.*

BY H. E. BECKER AND F. W. NITARDY.

At the suggestion of the U. S. P. Sub-Committee on Extracts, Fluidextracts and Tinctures, several formulas and methods for preparing Aromatic Fluidextract of Cascara were followed experimentally together with some modifications thereof.

The formulas suggested by the committee were:

	A.	B.	C.
Cascara Sagrada (crushed)*	1000 Gm.	....	....
Cascara Sagrada (coarse ground)	....	1000 Gm.	1000 Gm.
Magnesium Oxide	240 Gm.	150 Gm.	90 Gm.
Pure Ext. of Glycyrrhiza	40 Gm.	....	40 Gm.
Fluidextract of Glycyrrhiza	....	125 cc.	....
Gluside	2 Gm.	1 Gm.	1 Gm.
Glycerin	....	300 cc.	200 cc.
Alcohol	200 cc.	125 cc.	100 cc.
Flavor (for details see below)	....	....	....
Water to make	1000 cc.	1000 cc.	1000 cc.

* Coarse ground cascara was tried in formula "A" but found unsatisfactory as it clogged the percolator.

Formula "A" directed mixing the drug with the magnesium oxide and boiling the mixture with 6000 cc. of water for six hours; transferring to a percolator and percolating until exhausted; concentrating the percolate to 1000 cc. and adding sufficient ammonia water to give a distinct ammoniacal odor; then continuing evaporation to 700 cc. and adding the remaining ingredients, bringing the volume of the finished product to 1000 cc. by addition of water.

Formulas "B" and "C" directed moistening the cascara and magnesium oxide mixture with 2000 cc. of boiling water and setting the mixture aside in a percolator for 40 to 48 hours; then percolating. This amount of moistening liquid seemed to be excessive and interfered with even distribution or packing, thus resulting in poor extraction when both coarsely ground and crushed drug was used.

Because of the unsatisfactory results obtained, these experiments were repeated, using coarse ground drug and less water for moistening (1000 cc.) and allowing the drug to stand in a covered container for 24 hours before transferring to a percolator. With this modification, satisfactory flow and extraction were secured.

When the fluidextracts were finished, each was divided into four portions of 250 cc.

Three flavors were used in flavoring three portions of each fluidextract, the fourth portion being left unflavored.

Flavor per 1000 Cc.	1.	2.	3.
Oil of Anise	0.65 cc.	0.20 cc.	1.0 cc.
Oil of Coriander	0.15 cc.	0.15 cc.	0.1 cc.
Oil of Wintergreen	0.10 cc.	....	....
Fluidextract Angelica	....	....	2.0 cc.

* Section on Practical Pharmacy and Dispensing, A. PH. A., Toronto meeting, 1932.

The completed samples were labeled A-1, A-2, A-3, A-4,—B-1, B-2, etc., the letter indicating the formula used and the number indicating the flavor, No. 4 in each case representing the unflavored samples.

Odor and taste comparisons were made on unflavored as well as flavored finished products. The odor of the "A" series did not appear to be as clean and pleasant as that of the other fluidextracts. This difference in odor may possibly be due to the use of ammonia water at one stage of the evaporation after which a change in odor was noticed while the liquid was being concentrated. The odors of "B" and "C" were aromatic and clean, with "B" slightly smoother and less penetrating than the "C" series.

In tasting the unflavored samples the impression was gained that "A" might be preferable to "B" and "C," as three of five who tasted the products felt that "A" would make the best fluidextract. It also seems that the smallest amount of magnesium oxide (90 Gm.) is sufficient to satisfactorily debitterize the drug. (Confirms earlier work done in this laboratory.)

The larger amount of glycerin in "B" may be responsible for the smoother or softer odor and flavor of this preparation, also the glycerin content may be greater than is needed. Bringing the glycerin content of "C" to 25% seemed to make this sample smoother and apparently preferable to "B," while increasing its alcohol content seemed to make it taste warmer without otherwise affecting the taste.

Four of five people who tasted the flavored fluidextracts preferred the No. 3 flavor. We consider wider examination desirable to obtain correct choice of flavor, and further experiments with flavoring ingredient quantities may indicate that better combinations can be produced.

Two of the formulas directed the use of Extract of Licorice. Samples were obtained from three different manufacturers and quite a variation in odor, color and taste was noticed in these extracts. We therefore suggest the use of Fluidextract of Licorice instead of the extract, as we believe it will lead to greater uniformity in taste and appearance.

Experience in this laboratory has shown that 10% of alcohol satisfactorily preserves this preparation, hence we consider it sufficient.

In addition to preparing the foregoing fluidextracts we determined the total solids in 10 cc. of percolate of fluidextract strength when cascara-magnesium oxide mixtures were extracted by methods analogous to those given under experiments "A," "B" and "C."

	A. Crushed Drug.	Crushed Drug.	B. Coarse Ground Drug.	Crushed Drug.	C. Coarse Ground Drug.
Determination I	3.22 Gm.	2.31 Gm.	3.08 Gm.	2.52 Gm.	3.18 Gm.
Determination II	3.20 Gm.	2.32 Gm.	3.09 Gm.	2.55 Gm.	3.08 Gm.
Average	3.21 Gm.	2.315 Gm.	3.085 Gm.	2.535 Gm.	3.13 Gm.

Crushed bark (as used in "A") and coarsely ground bark (as used in "B" and "C") mixed with 240 Gm. of magnesium oxide per 1000 Gm. of drug were also extracted by extraction methods as used in "A" and "C," respectively, and total solids determinations made on the percolates concentrated to fluidextract strength with the following results:

Process "A" (crushed bark)	3.21 Gm. in 10 cc.
Process "C" (coarse ground bark)	3.22 Gm. in 10 cc.

Hence from the standpoint of extraction efficiency the two methods are equally good, providing percolation is carried to exhaustion of the drug. Percolate from "A," however, was lighter in color even though its extractive content was the same. Therefore, it appears that the magnesium oxide affects the very coarse crushed drug differently so far as color is concerned than the less coarse ground drug. More rapid extraction was apparent in "C" as indicated by a higher total solid content in the first percolate taken from the drug.

During percolation, difficulty was experienced with clogging of percolators in two of four trials with the method of boiling the crushed drug (Method A). This method appears to be suitable for large scale operation but for smaller scale production we suggest the moistening of 1000 Gm. of coarsely ground drug and the required magnesium oxide with 1000 cc. of boiling water and allowing it to stand in a covered vessel for 24 hours before packing in a percolator.

Our experiments and observations lead us to suggest the following formula as one worthy of consideration in further experiments:

Cascara Sagrada, in coarse powder	1000.0 Gm.
Fluidextract of Licorice	125.0 cc.
Magnesium Oxide	90.0 Gm.
Gluside	1.0 Gm.
Glycerin	250.0 cc.
Alcohol	100.0 cc.
Oil of Anise	1.0 cc.
Oil of Coriander	0.1 cc.
Fluidextract of Angelica	2.0 cc.
Water to make	1000.0 cc.

Mix the cascara with the magnesium oxide and moisten in a dish with 1000 cc. of boiling water. Cover the dish and allow to stand for 24 hours. Transfer to a percolator and percolate with boiling water until the drug is exhausted; evaporate the percolate as received to 500 cc. When cold, add the glycerin and the alcohol in which the gluside and flavoring ingredients have been previously dissolved. Finally make the preparation up to 1000 cc. with water.

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THE THERAPEUTIC ACTION OF PYRULARIA OLEIFERA.*

BY JOHN WIECZORKOWSKI AND L. K. DARBAKER.

Pyrularia oleifera A. Gray has been given a number of common names: Crazy nut—it is said to be given to demented persons to make them sane; mother-in-law nut—said to be one way in which to eliminate mothers-in-law; and oil nut—probably on account of the large oil content of the fruit which contains 61.94% of an acrid fixed oil.

Pyrularia oleifera is a member of the *Santalaceæ* and its habitat is in rich mountain woodlands in the Alleghenies, south of the Mason-Dixon line. It

* Scientific Section, A. PH. A., Toronto meeting, 1932.

grows as a shrub, ranging in height from one to four meters. When young the whole plant is downy but when older, glabrous; probably this accounts for the older species name "pubera." The leaves are oblong, acute, more or less pointed at both ends, soft, very much veined and minutely pellucid punctate. The flowers occur in June and are greenish yellow, small in size and occur in terminal racemes. The male flower contains four to five short stamens, while the fertile flowers contain a pear-shaped ovary.

The fruit is yellowish in color, fleshy, drupe-like, pear-shaped, one-seeded and averages 2.5 cm. in length. The embryo is small and very oily.

Specimens used in our investigations were collected at Ohio Pyle, Pennsylvania, the only recorded stand north of the Mason-Dixon line.

Fluidextracts were made from both the whole fruit and the separated kernels without previous drying.

The investigations resulted as follows:

Fluidextract from the whole fruit.

Administration: Hypodermic, intraperitoneal. *Dose:* 0.003 cc. per Gm. weight of guinea pig. *Results:* General convulsions within three minutes, followed by general paralysis and usually complete recovery in 24 hours.

Administration—*Per os: Dose:* 0.003 cc. per Gm. weight of guinea pig. *Results:* Convulsions and death within an average of 18 minutes.

Fluidextract from the kernel.

Administration—*Per os: Dose:* 0.003 cc. per Gm. weight of guinea pig. *Results:* Convulsions and death within 60 minutes.

From this incomplete investigation it would seem that the fruits of *Pyrularia oleifera* are very poisonous. It is hoped that further investigation may be carried out. The toxic principles should be determined as well as the physiological action of the oil.

PIONEERING IN PLANT CHEMISTRY.*

BY ARNO VIEHOEVER.

Our present knowledge of plants and their uses has come to us down through the ages. Man, obviously by the trial and error method, early discovered the food, technical and medicinal value of plants and plant products. There is some evidence that only in modern times has man actually searched for the active and valuable ingredients.

Simple substances, as starch and cane sugar, were well known in antiquity. With the application of the general alchemistic methods employed in the middle ages: distillation, sublimation, melting, calcination, only the most resistant plant substances could be obtained, as benzoic acid, sublimed from gum benzoin. *Paracelsus*, the great independent fighter for medical science, endeavored to extract the active ingredients from medicinal plants, but the methods were still crude and the results rather unsatisfactory. Nevertheless, in 1675, *Lemery* gives us a grouping of chemical substances into mineral, animal, and vegetable products, and enumerates

* Section on Historical Pharmacy, A. PH. A., Toronto meeting, 1932. Illustrated by lantern slides.

among other plant products: sugar, turpentine, camphor, opium, gum benzoin and tobacco.

The great Swedish pharmacist, *Scheele*, probably deserves first mention as a pioneer, effecting or assisting in the isolation and purification of organic plant acids, as tartaric, citric, malic, oxalic and gallic acids, as well as the preparation of glycerin from olive oil (1784).

The work of the German apothecary, *Sertürner*, isolating morphine from opium (1805), that of the French professors of pharmacy, *Pelletier and Caventou*, isolating (1818 and 1820) other alkaloids as quinine from cinchona, created a real incentive for others to study the composition of plants. Thus we find in the 19th and 20th centuries a host of workers in the civilized countries of the globe engaged in the search for the active or valuable substances present in plants. Many workers should, no doubt, be classified as pioneers, had we the intimate knowledge of their life-work or the space to refer to it specifically.

Pharmaceutical workers, in the broadest sense, hold an honored place among the searchers in plant and drug chemistry. One of the outstanding men, a real pioneer, fruitful in his own work and in his inspiration to students and industries was the well-known German chemist, *Von Liebig*. His success during a lifetime, perfecting methods of organic analysis, and contributing greatly to the better understanding of the importance of chemistry in our life and in plant life (through soil fertility) furnish a lasting testimony. He may well be considered the founder of agricultural chemistry—soil and food chemistry.

In drug chemistry we meet frequently the name of *Dragendorff*, who, working in the Russian university (*of Dorpat*), elaborated an ingenious method for the successive isolation of plant constituents and assembled the data gathered by plant and drug chemists. The German educators, *Flueckiger* and *Arthur Meyer*, to whom I owe much gratitude for his teaching, the English, *Hanbury* and *Greenish*, the French, *Berthelot*, *Planchon* and *Perrot*, the American, *Maisch*, assembled valuable collections and data which brought them fame in the pharmacognostic field. *Trimble*, professor at Philadelphia College of Pharmacy, worked as a pioneer on the tannins, which group has in recent time engaged the attention of the most able chemists. *E. Schmidt*, of Marburg, Germany, my great teacher, author of the well-known "Handbook of Pharmaceutical Chemistry," spent a lifetime on the isolation of the alkaloids as the Solanaceæ, of Ephedra and many others.

Power with the splendid support of his friend *Wellcome*, a pioneer in medicine at-large, successfully completed a life-work of surveys, dealing with the intricate chemical composition of plants and drugs and fruit flavors.

Dean Kremers, the tireless worker, is surely in the front of pioneers of plant and drug chemistry, utilizing the State Experimental Plant Garden for fresh plant material to very good advantage. Outstanding, surely, is the work on the close chemical relation of pigments and flavoring substances demonstrated by him and his co-workers for the plant family, Labiatæ. Other American workers and especially the biochemists: *Gortner*, of Minneapolis, Minnesota; *McCollum*, of Hopkins; *Steenbock*, of Madison, Wisconsin; *Jones*, of Washington, should be in any list of prominent workers in the field of plant chemistry in the broadest sense.

Tschirch, the author of the well-known handbook of pharmacognosy, and *Dietrich* are authorities on the resins, a group still so little known. *John Uri Lloyd*

is the resourceful experimenter and manufacturer of unusual preparations, the inventor of an ingenious extraction apparatus; all command high respect for their achievements in plant chemistry.

Pioneer work is to be credited to the pharmacist, *Peckolt*, who went to Brazil and described many new drug products, to *Greshoff*, who made extensive surveys on plants, containing saponins and hydrocyanic acid, to *Molish*, the versatile professor of Plant Physiology in Vienna, to *Tunmann and Rosenthaler*, who collected data and devised new methods for the micro-chemical study of plants and drugs, to *Pregl*, who perfected the method of mino-analysis so useful in the study of plant compounds in living plants.

Our list would be all too fragmentary if we were to leave out the splendid work of such European pharmaceutical manufacturers as Merck & Company, on plant constituents; Schimmel, on essential oils; Hoffmann-La Roche, on preparations, the well-known American firms, etc.; of *Bourquelot* on the enzymes, active in the hydrolysis and synthesis of plant compounds; of *Abderhalden*, on enzymes, proteins; of *Wallach*, the deceased Goettingen professor, on ethereal oils; of his successor, *Windaus*, on cholesterol, gallic acids, and digitalis; of the illustrious *Willstaætter* who solved the mystery of chlorophyll composition, a study which had engaged plant physiologists for a hundred years, of *Emil Fischer* who synthesized sugars and simple proteins; of *Wieland* who worked with marked success on vitamins and provitamins as the ergosterol; of *Warburg* for whom the Rockefeller Foundations created a new institute for the continuation of his remarkable studies on the metabolism of the plant and animal cell; he having explained the mechanism of chlorophyll action, storing light energy, and of iron serving as a catalyst in cell action—of *Bergius*, one of the most daring plant chemists.

Bergius, all but trumps nature in making new compounds in the hydrogenation of carbon, in the manufacture of food from wood, a veritable giant of applied science. Most of these workers were honored by the Nobel Prize.

Of foremost institutions, where pioneers in plant-chemistry labor, we mention the United States Department of Agriculture, the Plant Research Institute in Yonkers, New York, the Pharmacognostic Institute in Vienna, under the able leadership of *Wasicky*, of the Pharmacotherapeutic Institute in Leyden, Holland, directed by *Van Itallie*. The study of bio-chemistry is coming to the foreground and the work on insecticidal plants as pyrethrum by *Staudinger* of Zürich, as derris by *La Forge* of Washington, D. C., should be generally known as samples of new accomplishements.

It is a fact, generally little appreciated, that there is the greatest opportunity for pioneer work in Plant Chemistry. The chemistry of the living drug plant is still a mystery in most cases.

It is an open question how thoroughly much of the work now on record has been done—with dried specimens, with small lots, with crude methods then available. "The science of drugs is hardly known," said Sir Henry S. Wellcome recently, "only the surface has been scratched." The chemical knowledge of such well-known drugs as Aloes, Cascara, Rhubarb, Podophyllum and Digitalis, to mention but a few examples, and their standardization is still unsatisfactory.

We attempt to contribute our humble bit, as time permits, to the work of the pioneers through the study of the living plants, wherever possible; the improve-

ment of selective extractions, checking the activity of the fractions with physiological test methods (preferably on transparent animals); the use of microchemical methods, and through the search for pure principles, and their study, physical, chemical and physiological.

Pharmacy is challenged, as a calling, to help the medical profession in providing the perfect medicine. Pharmacy can meet this challenge through pioneering in the Biochemistry of plants and animals yielding—per chance—the healing sap or substance for the helpless sick.

PUBLICITY FOR PHARMACEUTICAL EDUCATION.*

BY C. W. BALLARD.

It is difficult to definitely place the responsibility for the decline in prestige of retail pharmacy in the public mind. The replacement of individually owned establishments by those of large organizations concerned primarily with the business aspects, the diminishing number of prescriptions and the excessive number of pharmacies in the larger centers are all undoubtedly factors in creating the situation. But be the causes what they may, the fact remains that pharmacy is further away from a professional status than it was a generation ago. It must also be conceded that other professions and notably dentistry have materially increased in the public estimation. This decline in prestige cannot be charged to a diminishing of the educational standards, for in this respect pharmacy has kept fair pace with other professions. But the public as a whole knows nothing regarding the educational preparation for the practice of pharmacy. Education, both general and professional, is taken for granted in medicine, dentistry and law, perhaps in part because of the professional attitude assumed toward the public by those in these professions. Pharmacy is most often typified in the public mind by the luncheonette type of store where the professional aspects are almost wholly submerged. The task of rehabilitating pharmacy in popular estimation involves education of the public and it cannot hope to succeed without close coöperation on the part of the retail pharmacist. In its relationship to the public this educational project or campaign presents three phases—the individual pharmacist, the press and the pharmacy schools. Concerted action on the part of all three is necessary for a satisfactory culmination and the efforts must be maintained for a considerable length of time.

THE PHARMACIST AND THE PUBLIC.

The individual pharmacist is the most immediate point of contact between the public and pharmacy and he, undoubtedly, can do the most effective work in this educational project. Unfortunately, he is often apathetic in his attitude and is apt to regard professional pharmacy as limited to the compounding of prescriptions. Because of the diminishing number of prescriptions he feels that his claims to professionalism are correspondingly diminished. He readily sees the fallacy of rating the professionalism of a physician by the number of patients he visits, the dentist by the number of teeth he extracts and the lawyer by the number

* Section on Education and Legislation, A. PH. A., Toronto meeting, 1932.

of cases he handles in court, yet he still holds firmly to the number of prescriptions as the only index of his professional status. He realizes, as we all do, that under present conditions a community cannot support more than a few establishments exclusively devoted to compounding. The tradition is so strong that this lack of prescriptions may be the basis for the inferiority complex with which the retail pharmacist is frequently afflicted. While not discounting compounding as a mark of professional status, there are numerous phases of retail pharmacy which can serve the purpose equally well. Display of licenses is admittedly a small matter, but the very fact that the pharmacist is a licensed person at once segregates him in the public mind from the butcher and the grocer. Formerly these licenses were displayed in a conspicuous place, often in the show window, and they were accompanied by college diplomas. I venture to say that at present, licenses and diplomas while legally displayed, are not placed where they will catch the public eye. In the office of the average physician or dentist these evidences of his professional education are usually displayed. Window space is valuable but licenses and diplomas are not bulky. Perhaps they will pass unnoticed but there is also the possibility that, because of their scarcity in the modern store window, they will attract public attention. At any rate there is little liklihood of invidious comparisons being drawn between corporation and individually owned stores in such a feature, for the former seldom employ more registered pharmacists than necessary to comply with legal requirements. The corporation store is primarily a business proposition and the bulk of the employees are salesclerks.

The idea of Pharmacy Week, conceived by the late Robert J. Ruth, has been very generally adopted as a means of conveying the professional aspects of pharmacy to the public. It is noteworthy that Pharmacy Week displays are not featured in the majority of corporation stores. While the Pharmacy Week plan is admirable, its chief defect lies in the fact that one week of such activity throughout the year cannot create a lasting impression. A manufacturer would hardly expect a one-week advertising campaign to produce year-round results, and likewise pharmacy cannot expect too much from a single week's efforts. There is nothing to prevent the pharmacist from more frequently making public display of the professional aspects of pharmacy and this would overcome this lack of continuity.

Much effort has been expended by pharmaceutical organizations in inducing physicians to prescribe more freely and to acquaint them with the official preparations. While this work has not entirely failed of its purpose, the results have been out of all proportion to the efforts. The physician, with his more ready approach to his colleagues, can accomplish more than the pharmacist in inducing medical men to prescribe more freely. The fact that he has no pecuniary interest in the matter is a decided advantage. Surely, each pharmacist is sufficiently familiar with at least one physician to present the case of official preparations and prescriptions as against proprietaries and counter calls. The element of personal contact is strong and although it requires diplomacy to gain the confidence of the physician, it can be done. I personally know of several instances where pharmacists are constantly consulted by medical men in prescription construction. The pharmacist of to-day generally has a broader knowledge of the articles of the materia medica than the physician and it but remains for him to show the latter what he knows about medicinal articles. In such relationships between pharmacist and physician it is quite

possible for the former to disseminate information relative to the modern pharmaceutical curriculum. I find that medical men have but little knowledge of the requirements for the practice of pharmacy and their respect for it increases when they are so informed.

Personality, attitude toward customers, dress and manner of conversation all play a part in instilling respect for pharmacy. Some of these are the characteristics which we term culture. Perhaps the inclusion of academic studies in the pharmacy curriculum may give our students these attributes but there is considerable doubt about its accomplishment in this manner. The so-called professional manner or attitude is not a subject of the medical or dental curriculum nor can it be in pharmacy. It is founded on the individual attitude toward one's calling, revolves about the respect he accords it and this in turn begets respect from the public. Our reaction toward the physician who appeared before his patients in shirt sleeves and without a collar would probably be decidedly unfavorable, yet this is the regular dress of some pharmacists in their stores. This type of pharmacist evidently thinks that professional status is not attainable because he is called upon more often for merchandise than for service. But modern merchandising stresses service and the pharmacist is advantageously situated to introduce this factor of service in a commercial transaction. A word of information regarding a product or a query as to the purchaser's preference will often pave the way for the pharmacist to display his professional knowledge.

THE PHARMACIST AND THE PRESS.

Pharmacists are generally poor advertisers of their activities. In the average small city newspaper we frequently see accounts of the meetings of local medical and dental societies and but rarely any notice of a pharmaceutical organization, if indeed one exists. My friends engaged in organization work are constantly bewailing the fact that their fellow pharmacists can with difficulty be induced to join the State associations and absolutely balk at local organizations. Reasons for this lack of *esprit de corps* include suspicion that the other fellow will benefit more from the association than they will, direct and personal antagonism to others in the same locality, a general feeling of "what's the use" and the tendency to be disappointed if direct personal results do not immediately follow their signing an application for membership. The number of names on the roster of any State pharmaceutical association, as compared with the number of practicing pharmacists in that state, illustrates the situation only too clearly.

Reporters are not, as a rule, assigned to cover local medical or dental meetings, but these organizations furnish matter for publication and it has sufficient news-appeal to be promptly printed. I can hardly believe that among the membership of a pharmaceutical body there is no person to undertake publicity work in a similar manner. In the smaller communities the press will usually give space to even the simplest notice, especially if it contains the names of business or professional men. Newspapers in the larger cities must necessarily limit the material for publication, but even here it is often possible to secure space if one can use matter of general public interest as the main theme and work in items of purely pharmaceutical import. Aside from newspaper publicity there remains the possibility of impressing the public as to the differences between the pharmacist and

the merchant by means of printed matter for distribution among his patrons. A typical folder of this sort issued by "Pharmacists' Educational Service," deals with the family medicine chest, names several U. S. P. and N. F. household remedies and concludes by calling attention in simple language to the qualifications demanded for the practice of pharmacy. The individual pharmacist might find it difficult to publish a series of this sort but an established organization could put forth this literature just as readily as they have supplied physicians with printed matter dealing with official preparations.

THE PHARMACY SCHOOL AND THE PUBLIC.

The last point of contact between the public and pharmacy is the pharmacy school, but unfortunately this contact, like that of pharmacy week, cannot be so readily and constantly maintained. On the other hand the schools are providing educational service and are therefore not directly financially interested. Teaching has always been regarded as a profession by the public, therefore the tie-up between pharmaceutical education and retail pharmacy may be more compelling than other means even though it be less constant. Nor need this work of education undertaken by pharmacy schools be entirely restricted to the general public for, and I think my teaching confrères will agree, members of other professions and especially other professional schools are frequently just as ignorant of the pharmacy school curriculum as the layman. At the very beginning it must be understood that a school in undertaking this work must devote its energies toward elevating pharmacy in the public eye. The public quickly senses any effort to commercialize this contact and an undue stressing of the desirability of pharmacy as a profession may easily negative the entire project, especially as regards press publicity.

The most feasible and perhaps the most impressive method for a pharmacy school to secure contact with the public is by means of an exhibit featuring the varied educational activities of the pharmacy curriculum. In planning an exhibit while each department or division can best select and arrange the features pertaining to its particular field, there must be a supervising head to coördinate departmental efforts and see that the entire project adequately represents pharmaceutical education. Lack of supervision may readily result in duplication, one-sided displays and the objectionable tendency to exhibit so much material that the visitor is overwhelmed. Exceedingly technical items or operations should not be stressed and the displays should possess a popular appeal. Apparatus, especially if it be in actual use as in a demonstration, always catches the public eye. Necessarily, explanatory placards or labels in nontechnical language should be liberally used. But a mere labeling of the exhibited material will not accomplish the full purpose. If the visitors are really interested they will ask questions and there should be a capable member of the staff present to give explanations. A greater interest can be aroused by having a staff member accompany a group through a given section of the exhibit, explaining the items displayed and inviting queries.

The exhibit project has been tried in but few of the pharmacy schools of the country and written reports of such activities are scarce. Last June the College of Pharmacy, Columbia University, held an exhibit of this sort and I am reporting the details of, and reactions to, this exhibit in the hope that data from other sources may be forthcoming. Plans for the project were considered for several months and

the work was placed in charge of a staff committee upon which were representatives from the three major divisions—Chemistry, Pharmacy and Materia Medica. Each of these divisions was given a free hand in deciding upon the details of their own exhibits. The committee supervised the whole so as to secure a degree of uniformity, prevent duplication and check the pardonable, but nevertheless objectionable, tendency of a given department to overload their particular section and thus monopolize attention. Owing to this exhibit covering all six floors of the College building with eight large laboratories and a library, all used for the purpose, it was necessary to organize the teaching staff and the laboratory helpers so that visitors could be systematically shown through. A registration book was kept for the signatures of visitors and printed catalogs of the exhibit were distributed at the entrance. The catalog was descriptive of the type of exhibits displayed on each floor and by being so arranged, a visitor with limited time or interests could make his own selection and be directed accordingly. Every effort was made to have those attending spend at least a short time on each floor so that all phases of pharmacy might be seen.

A specific description of each part of this exhibit would be impossible within reasonable time limits, but an idea of the general plan and the types of materials and apparatus shown can be gained by reference to the following excerpts from the printed catalog.

Main Floor

Library.—Rare 15th century pharmaceutical books and utensils; special reference books and current journals in the fields of pharmacy, chemistry, materia medica and allied subjects.

A Modern Model Pharmacy.—Prescription department; ethical specialties; biologicals.

Dispensing Laboratory.—The compounding of prescriptions: pills, capsules, troches, tablet triturates, powders, ointments, solutions, emulsions, etc.; what goes into the prescription.

Sub-Level—The Pharmacy of 1829.—A model pharmacy of one century ago with original equipment and materials.

Second Floor

Physics Laboratory.—Photo-electric cells; radio-wave apparatus and tubes; X-ray and cathode ray demonstrations; radio-activity exhibit; spectroscopes; spectrophotometer; color analysis; polariscopes; refractometers; instruments for the analysis of oils; electrometric determination of p_H; conductivity apparatus and exhibits in mechanics, wave motion and heat.

Fourth Floor

Materia Medica Laboratory.—Displays of fresh and dried crude drugs; microscopic views of powdered drugs; living drug plants in terraria; glandular products and biologicals; living animals used in biological assays; models, charts, X-ray pictures and actual specimens of human organs; cryptogamic specimens including interesting fungi; drug and spice maps of the world; microanalysis of foods; evolution of microscopes and models from 1788 to date; methods for sectioning and the preparation of slides; pharmaceutical sundries and first-aid equipment; poisons and their antidotes.

Bacteriological Laboratory.—Sterilizers and autoclaves; cultures; microscopic views of pathogenic bacteria; vaccines and serums; evaluation of antiseptics; dark field illumination; photomicrographic equipment; parasitology exhibit; chemical analysis with the microscope; apparatus for the chemical and microscopic examination of blood and urine.

Fifth Floor

Pharmaceutical Laboratory.—Apparatus used in pharmaceutical processes; demonstrations of crystallization, extraction, percolation, sublimation; manufacture of scale salts, solutions, tinctures, mulls, medicated gauzes, U. S. Pharmacopœial and National Formulary preparations.

Pharmaceutical Manufacturing Laboratory.—Manufacture of organic medicinal chemicals showing processes of steam and vacuum distillation, reflux condensation and extraction; display of natural and synthetic perfume materials together with those used in cosmetic manufacture; exhibit showing the use of ultraviolet rays in chemical and pharmaceutical analysis.

Sixth Floor

Chemical Laboratory (Organic).—Medicinal chemicals derived from coal tar, petroleum, wood, plants, animal tissues; newer synthetic remedies; special apparatus used in quantitative organic analysis; apparatus used in the analysis of water and foods with demonstrations; apparatus and methods used in the testing of medicinal substances as oils, alcohol, alkaloids and official preparations for identity and purity.

Chemical Laboratory (Inorganic).—Chemical map of the United States; derivation of inorganic medicinal chemicals; processes and apparatus used in qualitative analysis and in volumetric, gravimetric and gasometric determinations.

Notices of the exhibit were distributed to the pharmaceutical, medical and dental press, to various educational institutions and the general public. During the five days of the exhibit well over 1300 persons registered in attendance, excluding duplications occurring through visitors returning with others. Among those attending we find physicians, dentists, nurses, teachers, science clubs, nature study groups, chiropractors and students at various schools, both academic and professional, and pharmacists. An interesting development of the project is the request for talks or lectures before groups interested in some particular phase. Such groups are perhaps not interested in pharmacy but the very fact that they invite members of a pharmacy staff to address them contributes something toward raising pharmacy in their estimation.

The question may well be asked as to what an exhibit project does for pharmaceutical education and ultimately for pharmacy. Perhaps the most frequently repeated phrase heard by members of the staff during the exhibit was, "does the druggist have to study and know all this?" These ten words adequately express the ignorance, perhaps pardonable in view of the appearance of the modern drug store, that prevails among persons in various walks of life, regarding pharmacy and the pharmacist. Their very utterance betokens a more estimable opinion of the pharmacist than they previously possessed. A continuation of the work by this School and its adoption by others may well be a factor in the restoration of prestige to pharmacy and a greater regard for the pharmacist. The professional status of pharmacy has not been lost over night and neither can it be so regained by legislation or otherwise. The pharmacist must act and regard himself as a professional man before he can induce the public to so regard him.

COLLEGE OF PHARMACY, COLUMBIA UNIVERSITY.

1932 should give us some hint of the way to succeed and speak with authority. In a general way it has some false stars, slips, failures and regrets. May it be asked "What do the coming days and years hold for us, and wherein is success and whereby can it be attained?" "The same year that brought us many joys, and alas, many devastating sorrows and a host of enlarging experiences, must have a last gift for us—a garland for the ashes of regret."

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

"The question of whether students of pharmacy should be given fundamental courses in chemistry and later make the application of the chemical knowledge to pharmacy, or whether in such courses as qualitative analysis, quantitative analysis and organic chemistry the choice of material will be such as to give to the course a pharmaceutical significance, will probably never be settled. If students of pharmacy are taking these courses with other students in the University, naturally the instructor must give a general course. On the other hand, if only students of pharmacy are in the course, the instructor can very easily pick his material from the pharmaceutical world and thus make the course more practical. Some one has truly said that organic chemistry *is* organic chemistry and should be taught as such, regardless of whether the students taking it are enrolled in Science, Pharmacy, Agriculture, etc. Your Editor is inclined to believe that this is an extreme view to take on the subject and that, in the case of a class composed entirely of students in any one school, the course should be made as practical as possible for the work that these students are expected to follow after graduation. The following paper on 'The Scope of a Course in Organic Pharmacy' will be interesting to all teachers of organic chemistry. I am not aware of any other college that gives a course known as 'Organic Pharmacy.' However, such a course is probably necessary and valuable, if the organic chemist treats his subject from the purely scientific standpoint."—C. B. JORDAN, *Editor*.

THE SCOPE OF A COURSE IN ORGANIC PHARMACY.*

BY ANTOINE E. GREENE.[1]

The proper division of the subject matter of the present course in pharmacy offers a problem which is well worth the serious consideration of the teaching profession. Then after the division comes the necessity for a systematic arrangement of course material, based first upon general instructional necessity, and, secondly, upon local attitude toward specific instruction.

In general we may commence by dividing pharmaceutical instruction into those subjects coming under the following heads:

1. Pharmacy. 2. Chemistry. 3. Materia Medica—Pharmacognosy. Pharmacology. 4. Related Subjects. 5. Cultural Subjects.

Under the last two heads we might place such subjects as physiology, bacteriology, botany, mineralogy, physics, economics, psychology, English, the foreign languages, etc.

Under the general heads of Pharmacy, Chemistry, etc., we may conveniently separate them into major and minor or accessory courses. For instance, pharmacy might be divided into theoretical, practical, dispensing, inorganic, organic, commercial pharmacy, etc., as majors, while the minor or accessory subjects would naturally embrace pharmaceutical mathematics, Latin, history, seminar, etc.

Now as to the subject of this paper, we naturally consider organic pharmacy to be a major division of pharmaceutical instruction, devoted to a comprehensive study of those organic compounds which are official in the United States Pharma-

* Delivered before the Teachers' Conferences on Chemistry, Toronto meeting, 1932.

[1] Associate Prof. of Pharmacy, Howard University, College of Pharmacy, Washington, D. C

copœia, Decennial Revision, and the National Formulary, Fifth Edition. Sufficient attention, time permitting, should be directed to those new and non-official organic medicaments of therapeutic and pharmaceutical importance and interest.

We draw off all of the organic compounds from the official standards and group them according to an orderly chemical classification. It has been found convenient to use the order set down in "Elements de Pharmacie," by Andouard and Pastureau (Latest Edition, Paris). That is, we take up the study of the hydrocarbons of the aliphatic series, then the halogen derivatives, the alcohols, ethers, aldehydes, ketones, acids, esters, amines and amides, sulphur compounds, amino acids, proteins, carbohydrates and enzymes. Turning, then, to the aromatic hydrocarbons, we follow a similar procedure.

Although pharmacy is permeated with chemistry and chemical applications, we assiduously avoid giving our course too much of a chemical flavor. It is so easy to steer the course into dangerous waters by teaching not wisely, but too well. It is questionable whether the teacher in pharmacy is at all equipped to teach organic chemistry, particularly the organic chemistry of these fertile times. To the chemist belongs the responsibility for thorough instruction in the fundamentals of theoretical and practical organic chemistry. Organic Pharmacy deals in no way with complicated syntheses, involved reactions or elaborate formulas. The scope of organic pharmacy is to emphasize the salient facts concerning those organic medicaments of pharmaceutical and therapeutic importance. And the instructor of such a course will find his time well taken up gaining a whosesome familiarity with the hundreds of medicinals which have crowded the medicamentarium.

It is manifestly absurd to expect the professor of organic chemistry to pause and point out the pharmaceutical applications of the malonic acid ester and acetoacetic acid ester syntheses in large, mixed classes. In our course in organic pharmacy, the student is given some insight to the pharmaceutical utilization of many of these important synthetic reactions, which he once learned long since and then forgot awhile.

There is frequently the danger of serious departmental incompatibility arising because of fundamental ignorance in the necessity for adequate pharmaceutical instruction. The department of chemistry, in particular, may unfortunately suffer from the erroneous belief that the pharmacy department is attempting to reteach chemistry or to impart wrong notions of chemical principles. We have had such an unfortunate misunderstanding in our own University. After an enlightening series of conferences, however, the difficulties were ironed out, and an *entente cordiale* established. The instructional corps in organic chemistry considers our course in organic pharmacy no more a purely chemical subject than we deem their course in chemical preparations a branch of inorganic pharmacy.

The Pharmacopœia and National Formulary would hardly fill the need of our students in organic chemistry. We would be hopelessly lost if we had to use a Richter, Cohen or Norris in teaching organic pharmacy. The Pharmacopœia is our "Bible;" the National Formulary is our "prayerbook."

It is obviously impossible to make a detailed study of all organic compounds of therapeutic importance or pharmaceutical value. We can only confine ourselves to the most important. By continually focusing the attention of the student upon

the organic materials which he uses daily in prescription and laboratory practice can we meet with a modicum of success.

There may be some unnecessary duplication of subject matter, but by extra departmental conferences and course analysis, such repetition may be reduced to a minimum. Then, a certain amount of repetition of important subject matter may be considered not only wise, but valuable. Such time is surely not wasted.

The value of the course may be determined by ascertaining how much better the student is acquainted with the organic materia medica than before. This may be found out through written and oral examinations. In pharmacognosy and galenical pharmacy we examine the students on their knowledge of the drugs and preparations with which they come in contact daily. We expect them to recognize by color, odor, taste and feel a large number of crude drugs. As they proceed in the identification of numerous specimens, we expect the recognition to strike responsive chords in their memories as to definition, official descriptions, impurities, constituents, doses, uses and preparations into which the drug enters. Some may throw up their hands in horror at such archaic methods of instruction. But in the greatest number of cases, pharmacognosy is still so taught.

Likewise, in organic pharmacy, we expect our students to differentiate thymol, camphor, menthol and chloral hydrate. While trichloracetic acid is derived from trichloroaldehyde, we expect them to know it from the generic aldehyde. There are a large number of facts of pharmaceutical importance which should be brought to the attention of the student. Familiarity may breed contempt, but students cannot become too well acquainted with the material which they must daily handle. Because the physician and surgeon seldom use all of the anatomical knowledge of their student-days in daily practice is no reason why particular attention should not be placed on a sound, fundamental instruction in anatomy during the preclinical training. It is our firm belief that the course in organic pharmacy has a proper justification for its present place in the curriculum.

Some there are who would term such a course as organic pharmacy—pharmaceutical chemistry. The course as given includes no laboratory work. Specimens of official organic compounds are available for individual and collective study by the student. We encourage the student to become familiar with the physical and organoleptic characters of the material studied. The absence of laboratory instruction may be deplored, but, at present, we have neither time nor space for adequate laboratory instruction. Then, the additional laboratory work would justify calling the course Pharmaceutical Chemistry, since it would of necessity include qualitative and quantitative analysis of these medicaments.

It has been our experience to find that ninety-nine lecture and recitation hours are the optimum—minimum of time in which to cover the subject of organic pharmacy. Of course, we could use three times as many clock hours, but we are faced with the problem of overloading the curriculum. Just as there are those pests of the highway known as "road hogs," there are, in our colleges and universities, equally obnoxious individuals who might be termed "curriculum hogs." All of us have had contacts, often disagreeable, with the teacher who believes that his subject is the one and only part of the curriculum worthy of consideration. Therefore, we hope that our ninety and nine hours are not crowding other equally as important courses to the wall.

The instructor in organic pharmacy should visit all of the contributing departments of the course in pharmacy in an attempt to understand just where his field begins and ends. These visits may be productive of wholesome and worthwhile contacts. Too often the pharmacy department stagnates in its own isolation. With his own co-workers, he should have frequent contacts and conferences, seeking to develop a course which will round out and strengthen other courses which may touch his own. With free and open mind, he should be ready to receive both criticism and suggestion.

If he is so fortunate as to make the official organic compounds familiar to the students as the faces of their friends, he should call himself a successful teacher of his subject.

INCREASING PRESCRIPTION PROFIT POSSIBILITIES.*

BY FRANK A. DELGADO,** BUSINESS SPECIALIST.

"A paper by Mr. Frank A. Delgado needs no editorial introduction. The splendid work that Mr. Delgado did in the St. Louis Survey makes him an outstanding figure in pharmaceutical economics. The following paper on 'Increased Prescription Profit Possibilities' will merit the careful reading of any one teaching the subject or actually engaged in prescription business."—C. B. JORDAN, *Editor*.

It is generally customary when addressing a group of professional men to pay tribute to their profession. No one is more cognizant than myself of the debt civilization owes professional pharmacy. Pharmacy is the mother of medicine and the original source of many forms of research. Unfortunately, the achievements of pharmacists have frequently been credited to other activities. Pharmacy does not differ from medicine, law and other professions in the respect that it also has its economic side. This is the side with which the National Drug Store Survey is concerned.

Physicians, both "young" and "old," as regards length of practice, write more prescriptions containing official ingredients than proprietary ingredients. However, many "old" and "young" doctors individually showed decided preferences for official or for proprietary ingredients, the length of practice seeming to have no bearing on the particular choice.

There is hardly such a thing as a completely stocked prescription department. The pharmacist will require 325 different ingredients to fill the first 500 prescriptions compounded, the next 500 will require an additional 185, the third 500 an additional 118, and the fourth, fifth and sixth blocks of 500 will require 218 additional different ingredients or an average of approximately 73 different ingredients per block. Even after he has filled 8000 prescriptions, up to and including his ten thousandth prescription, he will be required to buy 31 new ingredients for every block of 500 prescriptions that he fills. Prescriptions written for items not in stock usually call for proprietaries.

Professional pharmacists charge less for prescriptions containing official preparations than those containing proprietaries.

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* An address delivered before the Teachers Conference on Pharmaceutical Economics, Toronto, Canada, August 22, 1932.

** Bureau of Foreign and Domestic Commerce.

From 34 to 41 per cent of the different ingredients used in filling prescriptions are proprietaries. However, their total occurrence is less than 20 per cent. The following facts are based on a questionnaire answered by the proprietors of 35 professional pharmacies scattered throughout the country, and are not based on the survey work in St. Louis. The inventory dollar value of a professional type pharmacy may range from $2000 or less to as much as $47,000.

Two out of three professional pharmacists detail their physicians. Ninety per cent of the professional pharmacists file manufacturers' literature relative to new specialities. They find it productive of results. They find that physicians utilize it. Ninety per cent of the professional pharmacists are on a manufacturer's direct list.

Twelve professional pharmacists state that 25 per cent or less of the prescriptions filled in their cities are filled by professional pharmacies. Ten other professional pharmacists state that 40 per cent or more of the prescriptions in their cities are filled in professional pharmacies.

Thirty-four professional pharmacists charge an average of $0.96 per prescription.

Physicians do dispense, or at least so say 31 proprietors of professional pharmacies; five other professional pharmacists say they do not, at least in their community. Twenty-four professional pharmacists are equally divided on the question of whether dispensing is increasing or decreasing. Thirteen say decreasing. Eleven say increasing.

The facts just stated are only preliminary and are not to be considered final but all are typical of those that will be contained in the planned second prescription report dealing with sales in professional pharmacies as contrasted with those made in the usual commercial type drug store. The first prescription report, dealing with prescription department activities in the usual commercial type drug store, has already been published. A third report dealing with operating cost and net profit in both types of establishment is also planned.

In order that pharmacy may better carry on its public health activities and render the community the maximum professional service, its members must be aided by having certain essential basic facts regarding business routine placed at their disposal. The purpose of the National Drug Store Survey is to place at the disposal of the druggists of this country a simple and practical method of determining the profit characteristics of any item in the drug store under the usual conditions of doing business.

Most of you are aware that I have principally concerned myself with that phase of the drug store having to do with the prescription department. You have already been supplied with one bulletin on this important phase of drug store operation and, as already stated, others will follow. No attempt has been made to show how prescriptions should be compounded for that is the task of the school of pharmacy. However, the attempt has been made and will continue to be made to show to what degree the prescription department is or is not profitable, and the endeavor will be made to point out how unprofitable operations in the prescription department may be avoided.

There is no question in my mind of the large potential benefit that the survey facts hold to those approximate 60,000 druggists already in business. In fact,

there is already concrete evidence of it having materially aided pharmacists now in business. I will mention just one instance. I have selected this particular example because it will illustrate how the survey has aided not only the drug business, but that department of the drug business which I am convinced is dearest to your hearts. I refer to the prescription department.

A Detroit retail druggist attended the National Drug Store Survey Conference held in St. Louis last April, and was impressed with the survey findings reported, for upon his return to Detroit he rearranged his prescription department with a resultant increase of 28 per cent in his prescription business.

The Detroit Office of the Bureau of Foreign and Domestic Commerce writes that three neighborhood drug stores on the East side in Detroit, including the store just mentioned, are planning on putting in a complete line of biologicals and entering into an active campaign for the physician's business.

If such a thing as the survey being of no great value to the approximately 60,000 druggists now in business were possible, the cost and labor connected with gathering the facts and figures that have been assembled would be more than justified in being made available to the student body of the many schools of pharmacy in this country, the graduates of which, I am informed, number approximately 2500 annually. I feel no hesitancy in stating my belief in the value of these economic facts to pharmacy students, for I am aware that this belief is corroborated by members of your "Conference of Teachers of Pharmaceutical Economics." Dr. O'Connell stated at the 1931 meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION at Miami, Florida:

> "The objection to business in a profession and disdain of monetary profit is losing ground in the minds of educators. Schools of pharmacy have failed to equip students to adapt themselves to their environment. The essential function of the pharmacist is professional, but the function of colleges should be broadened to include some economic instruction. If colleges do not meet this need willingly there will be danger of over-emphasis upon the economic aspect and that would be bad for the future development of pharmacy."

Another large group of druggists whom I feel sure would reap a substantial dollar and cent value from the survey reports, provided the wholesalers or some other group could place these reports in their hands in time, are the proprietors of the approximately 1750 new drug stores opened annually throughout the country. Furthermore, I understand that the number quoted is a low estimate and that it is below the average of the last five years, due to obvious reasons.

I wish to invite you and your pharmacist friends who can apply the survey facts in practical form to use the facilities of the Merchandising Research Division and the Chemical Division of the Bureau of Foreign and Domestic Commerce as the mediums through which may be obtained any facts regarding completed or planned phases of the National Drug Store Survey.

I would like to close by injecting a personal note into my remarks and state that if I were to again engage in pharmacy, I believe that my chances of success would be increased many times due to the survey facts regarding sound and unsound business practices that have been so forcibly brought to my attention.

NATIONAL PLANT SCIENCE SEMINAR.

WHY PHARMACOGNOSY?

BY EARL B. FISCHER,* CHAIRMAN OF PLANT SCIENCE SEMINAR.

If there is any single problem which confronts all teachers of Pharmacognosy alike, judging from discussions on teaching methods held at past sessions of the Plant Science Seminar and from conversations with individual members, it is the problem of how to present that subject in an interesting and attractive way. I do not presume to be an expert on the teaching of pharmacognosy but wish only to present a few ideas learned from a somewhat limited number of years of experience.

It may be said, and I believe without fear of contradiction, that the majority of students are not interested in pharmacognosy as much as they are in other phases of pharmaceutical study, such as pharmaceutical chemistry, operative pharmacy, dispensing practice, etc. In discussing the teaching of pharmacognosy and botany, Dean Teeters said: "Our professional student is interested in any subject in proportion to the use he can make of the information in his particular field." Many students, particularly if they have had drug store experience previous to college work, come to school with the impression that in every-day pharmacy practice little use is made, directly or indirectly, of information gained in pharmacognosy courses. They consider such courses as among the unnecessary evils of their work and are intent on getting by them as rapidly as possible, not realizing until after graduation that they passed up an opportunity for gaining considerable worth-while knowledge which can easily be put to good remunerative use.

In order to overcome this prejudice the younger teacher of pharmacognosy, I believe, is likely to attempt to justify his subject at the very outset of the course. In my judgment this is not the best procedure. To let the various phases of the subject justify themselves as the courses proceed seems to have a much more telling and lasting effect upon the student. Furthermore, a whole-hearted enthusiasm for his subject on the part of the instructor is considerably more effective in putting the work across than any attempt at justification in the beginning, and while this enthusiasm may not overcome entirely the disinterest on the part of some students, it will tend to make the subject less boresome to those whose interests lean naturally toward the other aspects of the pharmacy curriculum and even more interesting to those who may happen to like pharmacognosy. It is difficult, in face of the opposition to pharmacognosy which one encounters in students, practicing pharmacists and even in teachers of other pharmacy subjects, not to wonder if after all there is not some justification for their views. Any sharing of this prejudicial viewpoint must be guarded against, for, if acquired in the least degree, it is likely to be reflected in the work of the instructor; nothing is more quickly noticed than the least bit of laxity on his part in his work and the corresponding effect will be noticed in the students' response. On the other hand, to have a sincere interest in one's work is to be able to stimulate class interest and overcome in a large measure whatever prejudice exists at the beginning. I know of no other medium through which any one interested in or contemplating specializing in pharmacognosy can stimulate and increase that interest than attendance at sessions of this organization and by making use of the associations and intercourses thus made possible with those who have shown by a large part of their life's work their enthusiastic belief in the worth-while nature of their speciality.

There are a number of ways in which the presentation of pharmacognosy may be made more attractive. I do not mean, in what I have to say, to detract at all from the botanical aspect of the subject. We have heard much in various papers concerning the need for chemical reinvestigation of our vegetable drugs. We have found at Minnesota that the students are interested in any chemical aspect of pharmacognosy. This has given us the opportunity of using chemical demonstrations to arouse the students' interest. Such experiments as the acid hydrolysis of starch following the various stages from amylodextrin through erythrodextrin and achröodextrin and finally to the reducing sugar, glucose, with iodine and Fehling's tests, the precipitation and subsequent examination of osazone crystals, or the color tests for alkaloids, glucosides, cell-sap colors, etc., prove very striking and interesting. Most students, I believe, look to demonstrations such as these to break the monotony of time-consuming and patience-testing searches for some exceedingly elusive microscopic element.

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*Chairman's Address.

The isolation of a plant constituent such as a volatile oil, starch, inulin, a sugar or plant protein is also a valuable aid in holding a student's interest. These experiments can be selected so that they can be performed in a reasonable space of time and any experiment which ties the botanical or biological to the chemical side of pharmacognosy is of value.

Most students are aroused to interest when the matter of biological assay is mentioned and whenever such demonstrations are made. It is not difficult nor does it necessitate a great deal of equipment or time to demonstrate the effect of digitalis upon the heart of the frog or the cat, and the effect of ergot upon the cock's comb or the isolated uterus can be shown in a short space of time. Even though such demonstrations do not come within the scope of pharmacognosy proper and the teacher may tread upon the toes of the pharmacologist, there is no harm in using them in awakening the interest of the student pharmacist in the physiologically active vegetable substances he is called upon to handle during his professional career.

Much has been said in previous papers at these sessions concerning research possibilities in pharmacognosy. They have shown that such possibilities are practically unlimited in their scope. Work done on insulin with its suggestion of the possibility of some such principle being present in plants and similar work have shown the urgent need of a reinvestigation of the chemistry of vegetable drugs. The status of the botanical identity of such drugs as *Cactus Grandiflorus*, *Manaca*, *Cascara Amarga*, *Tonga* and *Psyllium* presents another line of reinvestigation open to pharmacognosists. It is not difficult for an instructor to gain the aid of some few students in carrying out in part, at least, the work on such problems. We have found that almost any student is willing to put in time outside his regular class work for the privilege of carrying on some experiment in plant cultivation, or some histological examination or biological assay, if he knows it is to be of value in adding to the general information on the subject concerned. In so interesting the student it is very likely that he may be induced to further specialize in pharmacognosy. The same might be said in connection with medicinal plant culture. Many of our Minnesota students are interested in the spring work of platting and transplanting our seedlings and watching them develop. When once started in such work, they find it both interesting and attractive.

Many more illustrations might be cited, such as the consideration of commercial applications of pharmacognostic principles to determinations of identity, purity and adulteration of commercial products, the history and romance connected with our vegetable drugs, most of which are ancient in their origin. It makes no great difference what is the nature of the factor introduced to enhance the study; the only requisite is that it awakens some sort of interest either in some phase of the study itself or in the monetary gain aspect.

One additional factor which makes the teaching of pharmacognosy difficult is the attitude of our state boards of pharmacy toward the subject. In some states, while the candidates for registration are required to identify and show a knowledge of a number of important vegetable drugs by macroscopic examination, they are seldom if ever asked questions concerning proper methods of preparation of such drugs as digitalis, belladonna, etc., nor are they expected to know very much about the official standards of purity and strength to which such drugs must conform. Yet they are expected to know how sulphuric acid or arsenic oxide and other chemicals are prepared. The examinations in pharmacognosy and botany of candidates for registration in England might well be followed in this country. It would seem that some united effort on the part of this organization might induce our boards of pharmacy to adopt some type of examination in which the individual candidate is required to know at least some of the outstanding and diagnostic microscopic elements found in our important vegetable drugs and standards therefor. The effect of state board examinations of this type upon students would be very helpful to any instructors in such a subject as pharmacognosy. Pharmacognosy is being recognized more than ever by our pharmaceutical educators as being an essential part of a board pharmaceutical training. This is evidenced particularly, I believe, in a report made to the American Association of Colleges of Pharmacy in Miami last year when its committee on Curriculum and Teaching Methods, in considering a paper by Dean Sturmer entitled "Remarks on the Four-Year Course," reported in part "that it is the opinion of this Association that a professional course in pharmacy is not planned as a preparation for a specific job; it is intended rather to provide a broad education which will prepare the student that he may have the resourcefulness to fit himself into any given job within the field of pharmacy and adjust himself better to the vicissitudes of life." If they recognize as worth while the training given the student by the pharmacy colleges of to-day, our

state boards should also recognize pharmacognosy as an important and essential part of a broad pharmaceutical education.

THE CONSTITUTION AND BY-LAWS OF THE NATIONAL PLANT SCIENCE SEMINAR.

Article I—Name and Objects.

This organization shall be called the Plant Science Seminar. Its objects shall be as follows:

To provide opportunity for:

1. The formation of acquaintanceships and the establishment of friendships with persons interested in Pharmacognosy, particularly Botanists working with drug plants, Phytochemists, Pharmacologists, Drug Collectors, Drug Growers, Drug Importers, Distillers of Volatile Oils and others interested in drug plants.
2. Acquiring a personal knowledge of drug plants (both wild and cultivated, living and in herbaria), and of the experimental and commercial production and handling of drugs in various sections of the United States and foreign countries.
3. The presentation (exchange) of knowledge along all pharmacognostical lines.
4. Personal investigative work or research under particular conditions, such as supplies of special materials, availability of special apparatus, the presence of specialized teachers, etc.

Article II—Membership.

The members of the Seminar are those persons interested in pharmacognosy, who have registered for two annual meetings of the Seminar and who have been approved for membership at a business meeting of the Seminar. Members only shall have the right to hold office or to vote. Associates are those persons who are not members but are registered at any annual meeting of the Seminar.

Article III—Officers.

The officers of the Seminar shall be a Chairman, a Vice-Chairman, a Secretary-Treasurer and an Executive Committee of five members consisting of the Chairman, Vice-Chairman, Secretary-Treasurer and two Past-Chairmen. The officers shall be elected annually from the membership, and shall hold office until the installation of their successors.

Article IV.

Amendments to this constitution can be made at any annual business meeting upon the recommendation of the Executive Committee and upon approval of two-thirds of the members present at the annual meeting.

BY-LAWS.

Article I—Duties of Officers.

The officers shall perform the duties customarily pertaining to their respective offices, shall report annually to the Seminar, and shall serve without remuneration. The Executive Committee shall arrange for the annual meeting and shall have charge of the business of the Seminar in the interim between the annual meetings. The Chairman and Secretary of the Seminar shall be the Chairman and Secretary, respectively, of the Executive Committee.

Article II—Fees.

There shall be no membership fee. There shall be a Registration Fee of an amount to be fixed annually by the Executive Committee and payable by those in attendance at each annual meeting.

Article III—Annual Meeting.

The annual meeting shall be held at a place convenient to and during the week preceding the annual meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION. The program for the annual meeting shall be of such a nature as to provide opportunity for (1) "botanizing" trips, (2) inspection or presentation in exhibits and lectures, of local plant industries, (3) "round-table" discussions on important pharmacognostical subjects, (4) social visiting. "Entertainment" and the expense of the program shall be kept at a minimum. Likewise provision shall be made for a minimum "living expense" for those in attendance.

Article IV—Publications.

The Executive Committee shall prepare a synopsis of the proceedings of the annual meeting for publication in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION and in such other journals as may desire it.

Article V—Amendments.

Amendments to these by-laws may be made at the annual business meeting upon the recommendation of the Executive Committee and approval of a majority of the members present at the annual meeting.

PAN-AMERICAN MEDICAL CONGRESS.

The fourth meeting of the Pan-American Medical Congress will be held in Dallas, Texas, on March 21st–25th. An elaborate program has been prepared and it is hoped to have a section on pharmacopœias. This is the first time that the Congress has held sessions in this country.

Surgeon General Hugh S. Cumming, Major General Robert U. Patterson and Rear Admiral Charles E. Riggs will attend. Surgeon General Cumming is president of the English Committee and Dr. Carlos Enrique Paz Soldan, of the University of San Marcos, Lima, Peru, of the Spanish Committee. Among others who will participate are Dr. John A. Farrell, associate director of the Rockefeller Foundation, international health division; Dr. Gegorio Arsoz Alfaro, of Beunos Aires; Dr. Octavio Montoro, of Cuba; Dr. Jose Torres Torija, Mexico.

Dr. Bolivar J. Lloyd, medical director of the United States Public Health Service, and Dr. Sergio Lazo Meneses, of Ecuador, are secretaries of the committees. **Dr. John O. McReynolds,** of Dallas, is president of the Congress.

There will be moving picture demonstrations and scientific and commercial exhibits. Also there will be clinics in all the hospitals of Dallas under the direction of the local profession participated in by visiting physicians. Two hundred members of the Pan-American League will serve as interpreters and associate sponsors.

TEXAS PHARMACEUTICAL ASSOCIATION.

The fifty-third annual meeting of Texas Pharmaceutical Association will be held in Galveston this year. Arrangements are under way for a large delegation of Texas pharmacists to attend the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION at Madison, Wis., August 28th–September 2nd. Indications are that a party, including members of families, of approximately one hundred will be made up. Aside from the greater interest which has been developed in Texas in the AMERICAN PHARMACEUTICAL ASSOCIATION this attendance is a compliment to former president, Walter D. Adams, who was recently elected member of the Council. Texas pharmacists have a fund well under way to equip and endow the editorial offices in the Pharmacy Building at Washington. An effort will be made to bring a succeeding meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION to Texas.

USE OF THE NATIONAL DRUG STORE SURVEY.

The Committee on Use of the National Drug Store Survey, at a meeting held in Washington, December 13th, decided that short articles emphasizing some of the important and valuable information contained in the *bulletins* of the United States Department of Commerce, relating to the survey, should be issued each month. A series of eight has been arranged for. **Dr. E. L. Newcomb** is secretary of the Committee.

The first *bulletin* sent out is entitled "Causes of Drug Store Failures." This is an analysis by the National Drug Store Survey Committee on "Use of Some of the Valuable Facts Revealed by the United States Department of Commerce," and should be helpful in studying business situations in drug stores. The complete *bulletin*, which is Commerce Bulletin No. 59, entitled "Causes of Failure among Drug Stores," by Victor Sadd and Robert T. Williams, can be obtained from the Superintendent of Documents, Government Printing Office, in Washington, for 5¢. The *bulletin* analyzes in detail the business histories of thirty drug store proprietors who had become bankrupt in recent years. Among the reasons for failure are high rents, lack of records and lack of analysis at various periods so that an understanding may be had of business conditions.

REPORT OF THE COMMITTEE ON UNOFFICIAL STANDARDS.

PLANTAGINIS SEMEN.

Plantago Seed.

Psyllium Seed—Plantain Seed.

The cleaned, dried, ripe seed of *Plantago Psyllium* Linné, known in commerce as French Psyllium Seed, or of *Plantago ovata* Forsk., known in commerce as Blonde Psyllium or Indian Plantago Seed (Fam. *Plantaginaceæ*).

It contains not more than 0.5 per cent of foreign matter, none of which is injurious, and all of its natural mucilage. It yields not more than 4 per cent of total ash and not more than 0.8 per cent of acid-insoluble ash.

Description and physical properties.—*Plantago Psyllium Seed.* Elliptical to ovoid, dark brown to reddish brown, shining, from 2 to 3 mm. in length and from 1 to 1.2 mm. in breadth, concavo-convex, with a longitudinal light brown area extending lengthwise along the center of the upper surface and a deep concavity on the lower surface in the center of the base of which is an oval, white hilum; when soaked in water the seed coat swells and the seeds become enveloped with a transparent mucilage free from taste and odor.

One part of seed occasionally agitated with 8 parts of water forms a thick tasteless mucilage.

Plantago ovata Seed. Broadly elliptical or ovate, boatshaped, pale grayish brown with a pinkish tinge, and with a dull surface, from 2 to 3 mm. in length and from 1 to 1.5 mm. in width; on the convex surface there is a small, elongated, shining, brown spot; on the concave surface is a deep excavation at the base of which is the hilum, covered with a thin whitish membrane; when soaked in water the seed coat swells and the seeds become enveloped with a transparent, colorless mucilage free from taste and odor.

One part of seed occasionally agitated with 15 parts of water forms a thick tasteless mucilage.

Structure.—Transverse sections cut through the center of the seed have a reniform outline and show a seed coat composed of a colorless epidermis of mucilaginous cells with more or less obliterated walls, a hyaline layer (in groove) and a brown pigment layer beneath which is a broad endosperm of thick-walled cells in the center of which is an embryo. Both endosperm and embryo possess aleurone grains of rounded, oval, pyriform or irregular shape from 2 to 8 microns in diameter and fixed oil droplets.

POTASSII THIOCYANAS.

Potassium Thiocyanate.

Pot. Thiocyan. Potassium Sulphocyanate, Potassium Rhodanate

Potassium Thiocyanate, when dried to constant weight at 110° C., contains not less than 99 per cent of KCNS. It contains not more than 3 per cent of water.

Description and physical properties.—Colorless, transparent, adherent, prismatic crystals. It is odorless and has a cooling, saline taste.

One Gm. of Potassium Thiocyanate is soluble in 0.5 cc. of water and in 12 cc. of alcohol at 25° C. One Gm. is soluble in 0.2 cc. of boiling water and in 8 cc. of boiling alcohol.

Tests for identity: The salt fuses at about 170° C. and at a higher temperature decomposes, finally leaving a white residue, which imparts a violet color to a non-luminous flame and is alkaline to litmus paper.

An aqueous solution of the salt (1 in 10) responds to the reactions for potassium and for thiocyanates, U. S. P. X, page 444.

Tests for purity: Dissolve 1 Gm. of the salt in 10 cc. of boiling alcohol: the solution is clear and free from undissolved residue.

Dissolve 1 Gm. of the salt in 100 cc. of distilled water, add 15 cc. of nitric acid and heat on a steam-bath for one hour: not more than 0.005 Gm. of precipitate is produced upon the addition of 1 cc. of silver nitrate T.S. (chloride).

An aqueous solution of the salt (1 in 10) meets the requirements of the test for heavy metals, U. S. P. X, page 439, and of the test for arsenic, page 428.

A 2-Gm. portion of the salt shows no more sulphate than corresponds to 0.5 cc. of fiftieth-normal sulphuric acid, U. S. P. X, page 462.

On heating the salt with a slight excess of sodium hydroxide T.S., ammonia is not evolved (ammonium salts).

Dissolve 1 Gm. of the salt in 10 cc. of distilled water, add 1 cc. of sodium hydroxide T.S., five drops of ferrous sulphate T.S. and one drop of ferric chloride T.S. Warm gently for one minute, acidify with diluted sulphuric acid, filter through white paper and wash well with distilled water: no green or blue color appears on the paper (cyanides).

Assay.—Dry about 0.2 Gm. of Potassium Thiocyanate to constant weight at 110° C. and weigh accurately. Dissolve in 100 cc. of distilled water and add 50 cc. of tenth-normal silver nitrate. Add 2 cc. of ferric ammonium sulphate T.S., and 2 cc. of nitric acid and titrate with tenth-normal Potassium Thiocyanate. Each cc. of tenth-normal silver nitrate corresponds to 0.009717 Gm. of KCNS.

Preserve in tightly stoppered glass containers free from iron. The salt must not be exposed to contamination with even traces of iron, which might occur in dust.

AVERAGE DOSE: Metric 0.3 Gm.—Apothecaries, 5 grains.

ACIDUM MALICUM.

Acid. Malic. Malic Acid

Malic Acid contains not less than 99.0 per cent of $C_2H_3(OH)(COOH)_2$.

Description and physical properties.—A white or nearly white, crystalline powder, which is stable in dry air. It is odorless and possesses a distinct acid taste.

One Gm. of Malic Acid dissolves in approximately 0.7 cc. of water at 25° C. It is freely soluble in alcohol and ether.

Tests for identity: An aqueous solution of Malic Acid 1 in 20 is strongly acid to litmus paper.

A concentrated aqueous solution of Malic Acid after neutralization yields with several volumes of calcium chloride T.S. a white precipitate upon boiling. The precipitate is soluble in diluted hydrochloric acid.

When boiled with potassium dichromate and diluted sulphuric acid, Malic Acid evolves the odor of acetaldehyde.

Tests for purity: Upon ignition a 2-Gm. portion of Malic Acid yields not more than 0.3 per cent ash.

Ten cc. of an aqueous solution of Malic Acid 1 in 50 mixed with 0.5 cc. of hydrochloric acid meet the requirements of the test for heavy metals. (U. S. P. X, page 439.)

Ten Gm. of Malic Acid dissolved in 10 cc. of distilled water and set aside at room temperature for 3 days deposit no crystals (fumaric acid).

An aqueous solution of Malic Acid meets the requirements of the U. S. P. test for arsenic, page 428.

Assay.—Weigh accurately about 1 Gm. of Malic Acid and dissolve in about 30 cc. of recently boiled distilled water. Titrate the solution with half-normal sodium hydroxide using phenolphthalein T.S. as an indicator. Each cc. of half-normal sodium hydroxide corresponds to 0.0335 Gm. of $C_2H_3(OH)(COOH)_2$.

A speaker recently embodied the following in his remarks: "Unwisdom landed all the world into a bog of futility. My conception of the wisdom of life is simple—work with a will and with honesty, hope with a persistence that will paint the rainbow on the scene of 1933 even while you gaze on the foreground of it, and will give you the fortitude and the courage to go on and bear your burden yet awhile, for soon the better day approaches."

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

BALTIMORE.

A symposium on the National Formulary was the feature of the December meeting of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION, held at the Hotel Emerson, Thursday, December 22, 1932.

Chairman E. N. Gathercoal, of the National Formulary Revision Committee, was the principal speaker and had for his subject "The Progress of the Sixth Revision of the National Formulary." Dr. Gathercoal's address dealt largely with the problems involved in revision and the manner in which they were met and overcome. Additions, deletions and retentions from the N. F. V were discussed. The time and labor involved in devising assay processes for new products were stressed. Perhaps the most interesting phase of the revision work was the method used by the Committee in ascertaining what products were sufficiently wide-spread in their use to merit inclusion. This information was secured by making an extensive prescription ingredient survey, in which each ingredient was tabulated according to the number of times it appeared in ten thousand prescriptions. By comparison of these values with those obtained in previous surveys, the status of the drug in question is readily demonstrated.

Professor Gathercoal stated that the progress made by this Revision Committee compares favorably with those of the past and it is expected that the new National Formulary will make its appearance in the latter part of 1935 or early in 1936.

E. F. Kelly discussed the Relationship of the National Formulary to the United States Pharmacopœia. He pointed out that the books, although on an equal legal footing, differed considerably in their make-up, and served somewhat divergent purposes. The U. S. P. has "therapeutic efficacy" and "established utility" as the basis of admission, the N. F. prepares formulas and guarantees standards for products having wide-spread use, based on the sound principle that any substance used as a medicament should be so controlled in the interest of public health and welfare.

In discoursing upon the "Relationship of the Official Standards to Law Enforcement," Dr. R. L. Swain traced the legal history of these volumes from their inception at which time they were self-imposed standards, to their present high authority as conferred by the National and State Food and Drugs Acts. He pointed out that a wider recognition of synonyms and a greater number of assays would enhance their value as instruments in the work of pharmaceutical law enforcement.

Messrs. Davidov, Kantner, Ragland and Williams spoke on the value of the National Formulary to the retail pharmacist. They emphasized the value of the book in dealing with the proprietary medicine evil and stressed the necessity of urging the physician to prescribe from its pages preparations of known composition and concentration rather than a proprietary whose recommendation comes from those most interested in its exploitation.

WM. F. REINDOLLAR,
Secretary-Treasurer.

CHICAGO.

The 209th meeting of the Chicago Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held December 13th at the University of Illinois College of Pharmacy.

President Terry opened the meeting, calling attention to the fact that the Chicago Branch was nearing the close of its 26th year of existence. He announced the appointment of the following members as the nominating committee for the officers of the branch for the year 1933: *Chairman*, Dean W. B. Day; I. A. Becker; Prof. E. N. Gathercoal.

The date for the January meeting was set for the evening of the 24th. On that date Professor Snow will discuss "Some Early Members of the Chicago Branch."

Mr. Webster, a member of the committee of the American Association of the Colleges of Pharmacy that is seeking to establish student branches of the AMERICAN PHARMACEUTICAL ASSOCIATION in the pharmacy schools, outlined the purposes of the student branches.

"Milestones of Research," a scientific talking picture produced and shown by the Eli Lilly Company, was presented to the large group assembled. The picture presented the manufacture of insulin from the crude pancreas to the biologically tested solution in the ampuls. The picture then showed the use of insulin on diabetic patients.

A rising vote of thanks was extended to the Eli Lilly organization for the presentation of this picture.

LAWRENCE TEMPLETON, *Secretary.*

DETROIT.

The November meeting of the Detroit Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held November 17th. The meeting was preceded by a dinner.

President Fleisher called the meeting to order. The minutes of the previous meeting were read and approved.

President Fleisher then introduced the speaker of the evening, Robert L. Whaley, of the Detroit Branch of the United States Department of Commerce, Bureau of Foreign and Domestic Commerce.

Mr. Whaley spoke on "The Application of the St. Louis Drug Survey and Its Relation to the Retail Drug Store;" he said this survey was made possible by the coöperation of the entire pharmaceutical industry. The survey has caused nation-wide interest.

Thirty-three associations contributed to the survey, which was made at the request of pharmaceutical associations. The cost of the survey was $75,000, one-third of which was paid by the U. S. Government, the balance was subscribed by pharmaceutical interests.

The survey presented some very interesting facts, particularly the great number of items necessary to completely equip the prescription department and the few that had every-day demand.

It was found that acetyl salicylic acid was by far the most commonly used prescription item. Sales in other departments were found to increase the volume considerably, without adding to the cost of operation. This was found particularly true with toiletries, candy and the soda fountain.

Drug store failures were found to be due to high rentals and poor locations; stores paying rentals up to 5% of volume were successful while those paying 10% were unsuccessful. Many other interesting points were brought out by Mr. Whaley; complete data pertaining to the Survey may be had by applying to the Department.

Clarence Weaver, Prof. Charles H. Stocking, of the University of Michigan, and Leonard A. Seltzer commented on the splendid work done by the Department; the Speaker was given a rising vote of thanks.

Mr. Seltzer moved, seconded by Mr. Weaver, that the Detroit Branch of the A. PH. A. go on record supporting the movement which requires graduation from a recognized College of Pharmacy before applicant can take the Michigan State Board of Pharmacy examination.—Carried.

Mr. Seltzer then moved, seconded by Professor Dorion, that the Detroit Branch recommend Bernard A. Bialk to Governor-Elect William A. Comstock to fill the vacancy on the Board of Pharmacy, which occurs December 31, 1932.—Carried.

BERNARD A. BIALK, *Secretary.*

NEW YORK.

The December meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the Brooklyn College of Pharmacy, on the 12th, President Fischelis taking the chair. There was an attendance of about 65.

The president expressed the thanks of the Branch for the kind invitation extended by the Society for the third successive year to hold a meeting with its members.

The minutes of the November meeting were presented in abstract by the secretary and were approved.

At this point in the program Dr. Fischelis introduced Mr. J. D. Hill, a representative of the Emergency Unemployment Relief Committee, who spoke of the work of the Committee and appealed for support for its work.

Chairman Lehman, of the Committee on Education and Legislation, reported briefly on Federal and State legislation that was likely to be considered during the coming sessions. Dr. Mayer reported for the Audit Committee.

Joseph Rosin, of Rahway, N. J., was elected to membership in the Branch.

Mr. Heimerzheim reported progress for the Committee on Professional Relations.

The president appointed a Nominating Committee consisting of Joseph Mayer, *Chairman;* Hugo H. Schaefer and Robert Lehman.

Chairman C. W. Ballard, of the Committee on the Progress of Pharmacy, presented the following report: "The compilation of material for the forthcoming U. S. Pharmacopœia XI will undoubtedly reflect the progress of pharmacy in this country, but unfortunately the published list of deletions indicates a tendency toward medical progress at perhaps a more rapid pace than the practicing physician is willing to accept

The decision as to retention or deletion can no longer be based solely upon prescription use, but this factor should not be wholly cast aside. We are reminded that the first U. S. Pharmacopœia was for the guidance of the physician and it is only in later revisions that the pharmacist enters the picture. In 1907 the establishment of the Pharmacopœia as a legal standard brings the public into the matter as an interested party and one for whom the legislation is primarily intended. The constant deletion of articles which, although perhaps of doubtful therapeutic utility, are nevertheless demanded by the public, lessens the usefulness of the Pharmacopœia as an adequate public protective standard. The National Formulary may afford this protection by inclusion of such articles, but dismissal from the Pharmacopœia at once creates an impression that they are of secondary importance even if tons be used annually.

Deleted articles continue to be used by medical men and for this reason the results of prescription surveys should not be wholly ignored. Articles which have a wide-spread public use as home remedies and those which the patient is instructed, often by the physician, to obtain from the drug store should also be included. Typical examples are Anise and Fennel, both of which have been relegated to the Formulary as against Sumac Berries which still remains in the Pharmacopœia. A medical friend of mine jokingly suggested that it would be impossible to conduct a war without Compound Cathartic Pills.

Articles which are shown by prescription surveys or other referenda to be in use in 50% or over of the returns received should be retained. Articles in public demand should be restored and among these would be Anise, Fennel, Witch Hazel Water and Matricaria. All drugs noted as frequently used in the report of the Committee on Materia Medica, Conference of Boards and Faculties, District No. 2 should also be considered for inclusion.

Undoubtedly the physicians and pharmacists of this country desire to retain the privilege of pharmacopœial revision within their ranks, but an undue sacrifice of public protection to therapeutic usefulness and pharmacopœial necessity must eventually result in governmental intervention. Public as well as professional interests must be given consideration.

Following a discussion on Dr. Ballard's report, it was moved and carried that "The report of the Committee on the Progress of Pharmacy be sent in the form of a communication to the Committee of Revision of the United States Pharmacopœia as expressing the sentiments of the members of the New York Branch."

The president drew attention to the fact that at the January meeting Mr. Charles Wesley Dunn would speak on the subject of "Legislation to Outlaw Unfair Price Competition and Unfair Price Discrimination from Commerce." The meeting had been arranged with the coöperation of the Fair Trade Committee of the New York State Pharmaceutical Association, the members of which Association were being invited to attend the meeting.

President Fischelis then welcomed to the platform the speaker of the evening, Dr. Joseph A. Burgun, a pharmacist and a dentist, saying that the Branch had held joint meetings in recent times with physicians, but that this was the first time that a dentist had addressed the members.

Dr. Burgun's subject was "Dentistry and Its Relation to Pharmacy." The greater

part of the address dealt in a comprehensive way with the anatomy and the functions of the mouth, the teeth, and the relation to other parts of the body and how diseased conditions may result through lack of observation of healthy functions and neglect of mouth and teeth. It is regretted that space will not permit printing of this valuable address in full and an abstract would not do justice to the speaker. He spoke at some length relative to the proper prophylactic treatment and mouth cleansing. He stated that the use of a tooth-brush would not completely cleanse the teeth and other means were necessary for the purpose, such as floss.

Dr. Burgun referred to a formula by Dr. Herman Prinz for a dentifrice, as follows:

Precipitated chalk (light)	94 parts
Powdered castile soap	5 parts
Saccharin	1/20 part
Flavoring	1 part

He regretted misinformation relative to mouth washes and stressed the importance of seeing the dentist frequently, having the individual become acquainted with his condition and follow the dentist's instructions, and thereby prevent dental disease and its far-reaching ill-effects. He referred to the dental hygienist movement as an important service.

Dr. Burgun spoke of lime water, salt solution, sodium bicarbonate and perborate as mouth washes, and of a formula for a mouth wash powder composed of:

Saccharin	12 grains
Menthol	15 grains
Calcium oxide	150 grains
Sodium chloride	1 pound

Vice-President Bilhuber invited Prof. Frederick Schroeder, of the Brooklyn College of Pharmacy, to come to the platform to discuss the paper. Dr. Schroeder complimented Dr. Burgun; in his opinion the subject was so well presented that it needed no further comment. He remarked that years ago druggists alleviated toothache with various medicaments but that the intelligent pharmacist of to-day avoided treatment of this kind and instead sent the patient directly to a reliable dentist for care. If a toothache happens late at night the pharmacist may recommend that the cavity be dried with cotton and a little Oil of Clove be inserted on a pledget of cotton as a temporary expedient until proper dental care is available.

In connection with halitosis the speaker said that foul breath always comes from the mouth and head region and that it should be taken as a warning that something was wrong; it might implicate the teeth, tonsils, nasal sinuses, etc. It was formerly thought that a person had a foul breath because the stomach was out of order, and consequently, in the old days, the druggists usually gave cathartics. To-day they give mouth washes, but Dr. Schroeder felt that using a mouth wash was like trying to deodorize a garbage heap, and that if a perfect germicide was used it would probably destroy the tissues of the mouth. He held that mouth cleanliness was merely mechanical and that a person could not use a better tooth-cleaning agent than a simple tooth powder as suggested by Dr. Burgun. He felt that many tooth-pastes were exploited because of their financial reward rather than on real merit from a germicidal standpoint.

In connection with brushing the teeth Dr. Schroeder felt that the unhygienic tooth brush should be discarded and in its place suggested a one- or two-inch piece of sterile gauze wrapped around the index finger, moistened and dipped in the powder and then rubbed on the teeth. The only objection to this method was that it would be impossible to cleanse the occlusal or grinding surface properly. Dental floss is essential to dislodge food impacted between the teeth. For use as a general mouth wash he suggested 1/2 teaspoonful of salt in a tumbler of lukewarm water.

Dr. Schroeder then drew attention to the fact that the teeth were sources of focal infection for a large number of important diseases, and pointed out that in Class A institutions a routine medical examination always included a survey of the teeth by coöperating dentists. He concluded by saying that dental caries was not entirely due to neglect of the external care of the teeth, since some people at 90 who had never used a brush had perfect teeth; moreover, through the proper selection of foods, including the use of cod liver oil for vitamin D for calcification, much could be done to help protect the teeth from decay.

After a general discussion Doctor Anderson expressed the thanks of all present to Dr. Burgun; he was of the opinion that the pharmaceutical background had helped Dr. Burgun. Vice-President Bilhuber hoped that a joint meeting of the Branch and the Kings County Pharmaceutical Society would be held next year.

HERBERT C. KASSNER, *Secretary.*

PHILADELPHIA.

The December meeting of the Philadelphia Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held on Tuesday evening, December 13, 1932, at the Philadelphia College of Pharmacy and Science.

President Stoneback called the meeting to order at 8:15, and in the absence of the secretary, Mr. Bernard Melkon was appointed to act in that capacity for the evening.

Dr. Walter H. Hartung was introduced as the first speaker, and presented a lecture called "1:40, One Century of Organic Chemistry, Forty Centuries of Pharmacy." Beginning with the discovery of urea he described the manner in which organic chemistry has developed compounds helpful to medicine and modern life. He presented an interesting tabulation showing the number of substances classified as Inorganic, Biological, Natural and Synthetic that have been included as official from Pharmacopœias V to X. He said that of the approximately 400,000 known organic compounds about one in one thousand were useful in medicine, and suggested the need for further investigation of organic remedial agents.

President Stoneback then introduced Dr. D. M. Findlay who presented a paper on "Insulin, Its Manufacture and Use." Dr. Findlay displayed various specimens of pancreas and insulin. He stated that in the United States about 500,000 to 2,000,000 people are estimated to have diabetes, and described the disease with the symptoms and treatment. He also outlined for the audience the various steps in the manufacture and standardization of insulin, and related some of Dr. Banting's experiences in the development of the product.

At the close of the lecture, a discussion was held, the participants being Messrs. W. L. Cliffe, Wilmer Krusen, Harvey P. Frank and James C. Munch. The meeting was adjourned after a rising vote of thanks was tendered the speakers.

E. H. MACLAUGHLIN, *Secretary*.

Dean Townes R. Leigh has been appointed by the American Association Colleges of Pharmacy to the chairmanship of the Committee on the Establishment of a Pharmaceutical Corps in the U. S. Army. Dr. Leigh is Lieutenant-Colonel in the Chemical Warfare Service Reserve.

EMIL BOERNER HONORED.

The first dean of the Pharmacy College of the State University of Iowa, Emil Boerner, was given a dinner on December 15th, at the Memorial Union building of the State University. Senator J. M. Lindly, a former student under Dean Boerner, presided as toastmaster and the occasion was enhanced by the presentation of a portrait of the honor-guest to the University; a sketch of the veteran pharmacist will be found in the August number (1927), of the JOURNAL A. PH. A., page 709. Dr. Boerner was a member of the committee to draft the constitution of Iowa Pharmaceutical Association; he taught in the Iowa College of Pharmacy from 1882–1884, and was elected dean of the College of Pharmacy when it became part of the University.

Among the speakers were Dr. Rockwood, of the Chemistry Department of the University; Dr. Jessup, president of the University; B. F. Osborn, president of the Iowa Veteran Druggists' Association; E. L. Beezley, president of Iowa Pharmaceutical Association; J. W. Slocum, of the State Board of Pharmacy, Dean Wilber J. Teeters, Prof. Zada M. Cooper and others. Many congratulatory telegrams were received.

BRIGADIER GENERAL WARFIELD.

Brigadier General Edgar Warfield celebrates his 91st birthday, June 7th. At the age of 15 years he engaged in a drug store; three years later he left Alexandria, Va., with 700 others, to join the Confederate forces, few of whom returned after the 4 years of service. On his return, Mr. Warfield again entered the drug business, in which he has a record of 72 years. He was appointed on the first board of pharmacy of Virginia by the late General Fitzhugh Lee, when Governor of Virginia; he is honorary life president of the Virginia Pharmaceutical Association.

General Warfield is the sole survivor of the Old Dominion Rifles and is one of the oldest, if not oldest, active druggists in the country. He opens his pharmacy in Alexandria at 7:00 A.M. daily, and leaves the store at noon for the remainder of the day.

Annually, for more than thirty years, on the occasion of the celebration of General Robert E. Lee's birthday, the veteran pharmacist has recited the farewell address of the former to his troops.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1932–1933.

Office of the Secretary, 10 West Chase Street, Baltimore, Md.

LETTER NO. 5.

December 31, 1932.

38. Time and Headquarters for the 1933 Meeting. Motion No. 5 (Council Letters No. 3, page 1254, and No. 4, page 1358) has been carried and announcement has been made.

39. Local Secretary for 1933 Meeting. Motion No. 7 (Council Letter No. 4, page 1358) has been carried and Mr. Stanley has been advised of his election.

40. Election of Members. Motion No. 8 (Council Letter No. 4, page 1358) has been carried and applicants numbered 28 to 59, inclusive, are declared elected.

41. Contract for Printing and Mailing the Journal of the A. Ph. A. for 1933. The following letter has been received from Chairman DuMez of the Committee on Publications:

"I have checked over the bids for publication of the JOURNAL, obtained by Editor Eberle, very closely, and I am unable to discover how we would benefit by changing the publisher at this time.

"Some of the estimates are very near that of the present publisher, but the expenses in making a change would more than make up the difference.

"Editor Eberle informs me that the service has been entirely satisfactory, and I therefore recommend to the Council that the contract for publishing the JOURNAL for the coming year be renewed with the Mack Printing Company."

(*Motion No. 9*) *It is moved by DuMez that the contract for printing and mailing the Journal for 1933 be awarded to the Mack Printing Company of Easton, Penna.*

At the request of Chairman DuMez a vote is called for at this time but will be considered as tentative if there is objection.

42. Budget for 1933. Chairman Bradley of the Committee on Finance submits, in accordance with Article II of Chapter II of the By-Laws of the Council, the following report on appropriations and expenditures for 1932, with a suggested budget of receipts and appropriations for 1933, which were prepared by the Secretary and developed by the Chairman of the Finance Committee. The officers and Finance Committee are fully aware of the difficult times we are going through, which are resulting in curtailed receipts and many of the items in the proposed budget have been reduced, the total reduction amounting to more than four thousand dollars:

"To the appropriation for General Expenses in 1932, $25.00 was added for the Inter-Society Color Council, and $250.00 for Pharmacy Week Window Strips. The latter cost $137.50. We have also advanced $50.00 to the Committee on Pharmaceutical Syllabus, covering the appropriation for 1933. Of the appropriations, only three have been exceeded so far and all of these are within the $50.00 limit for which Council action is not required. They are the appropriations for Telegraph & Telephone, $209.52 against $200.00; Scientific Section $39.10 against $25.00, and Committee on Unofficial Standards, $65.00 against $50.00. We have made every effort to keep the expenses below the budget appropriations. Charges to December 1st were $20,083.81 as against $26,275.00 appropriated.

"Under the appropriations for open accounts to December 1st, the JOURNAL has cost $13,887.37 against the $11,000 appropriated, and the N. F. $2609.93 against the $1000. No charges were made against the appropriation of $1000 for Recipe Book or of $50.00 for Badges and Bars. Charges to December 1st were $16,497.30 against the $13,050.00 appropriated.

"To December 1st, the total budget charges were $37,581.11 against appropriations of $39,325.00, so we will probably not exceed our total budget.

"The receipts show considerable variation from the estimates. From Dues, $8571.88 as compared to $10,839.25 for the same period in 1931; in 1931 the receipts from dues showed a gain over 1930 of about 11%, and this year they are about 20% under 1931 so far. Every effort has been made to hold this figure up, but many explain that they cannot afford the expense. Bills for dues for 1933 were mailed on December 1st, and we cannot say what the total

for the year will be—anyway $2500.00 under the estimate. From the JOURNAL, $7862.34 as against $8335.26, which is very satisfactory under present conditions. From the N. F., $4143.27 for the year as against the estimate of $3500.00, which is very encouraging. From the Recipe Book, $1356.64 for the year against the estimate of $2500.00 which shows a decided decline. The receipts from interest on Headquarters Building Fund will be about $8500.00 as compared to the estimate of $5500.00, and this amount with what we may expect next year will approximately reimburse the ASSOCIATION'S outlay. $1000.00 was received from the U. S. P. Board of Trustees for the YEAR BOOK, and sales were $154.95.

"It will be necessary to use the net income for 1932, and possibly for 1931, from the Life Membership Fund, amounting to about $1560.00 or $3000, to balance our budget for this year. This income has not been used since prior to 1922.

BUDGET FOR 1933.

It is difficult to estimate receipts under present conditions. The following is suggested:

Interest	$ 100.00	
Dues	14,000.00	
Interest Life Membership Fund	1,600.00	
JOURNAL	9,500.00	
National Formulary	3,500.00	
Recipe Book	1,500.00	
YEAR BOOK	1,100.00	
Interest Headquarters Building Fund	4,000.00	$35,300.00

APPROPRIATIONS FOR GENERAL EXPENSES.

No. 1	Salaries	$10,800.00	
No. 2	Rent	900.00	
No. 3	Telegraph and Telephone	200.00	
No. 4	Clerical Expenses	1,400.00	
No. 5	Printing, Postage and Stationery	1,100.00	
No. 6	Office Supplies	150.00	
No. 7	Traveling Expenses	700.00	
No. 8	Premium on Bonds	50.00	
No. 9	Auditing	75.00	
No. 10	Certificates	50.00	
No. 11	Miscellaneous Expenses	100.00	
No. 12	Scientific Section	25.00	
No. 13	Section on Education and Legislation	25.00	
No. 14	Section on Practical Pharmacy and Dispensing	25.00	
No. 15	Section on Commercial Interests	25.00	
No. 16	Section on Historical Pharmacy	25.00	
No. 17	Commission on Proprietary Medicines	25.00	
No. 18	Committee on Local Branches	25.00	
No. 19	Committee on Membership	500.00	
No. 20	Committee on State and National Legislation	50.00	
No. 21	Committee on Syllabus	50.00	
No. 22	Committee on Unofficial Standards	50.00	
No. 23	Committee on Pharmacy Week	250.00	
No. 24	Inter-Society Color Council	25.00	
No. 25	International Pharmaceutical Federation	120.00	
No. 26	Metric Association	10.00	
No. 27	American Conference on Hospital Service	25.00	
No. 28	Headquarters Building Campaign	1,000.00	
No. 29	YEAR BOOK	3,750.00	
No. 30	Library	50.00	$21,580.00

APPROPRIATIONS FOR OPEN ACCOUNTS.

No. 31	JOURNAL:			
	(*a*) Publication	$9,500.00		
	(*b*) Clerical Expenses	1,000.00		
	(*c*) Postage and Stationery	300.00		
	(*d*) Freight, Drayage and Miscell	200.00	$11,000.00	
No. 32	National Formulary		1,800.00	
No. 33	Recipe Book		500.00	
No. 34	Badges and Bars		50.00	$13,350.00
				$34,930.00

"With these reductions it will be necessary to curtail expenses wherever possible, during the coming year. The reductions suggested will not, we believe, cripple the work of the ASSOCIATION to any extent. It will be necessary to keep the JOURNAL and National Formulary expenses within the appropriations, and this will mean abstracting or condensing many papers and articles in the former."

(*Motion No. 10*) *It is moved by Bradley that the budget for 1933 be approved as submitted.*

With the approval of the Chairman of the Council a vote is called for at this time. It will be considered as tentative if there is objection.

43. Selection of Auditors. The Chairman of the Committee on Finance recommends the employment of W. A. Johnson & Co., Baltimore, Md., to audit the accounts of the ASSOCIATION for 1932, in accordance with Article 8 of Chapter IV of the By-Laws. This Company has audited the accounts since 1922.

(*Motion No. 11*) *It is moved by Bradley that W. A. Johnson & Co. be employed to audit the accounts of the Association for 1932.*

44. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received.

No. 60, Hyman Aberback, 353 Ave. A., Bayonne, N. J.; No. 61, L. G. Gramling, Colonial Pharmacy, Orlando, Fla.; No. 62, Clarence A. Halm, 724 Miller Ave., Ann Arbor, Mich.; No. 63, William Howard Hunt, 2027 E. Preston St., Baltimore, Md.; No. 64, B. Montenegro, Rua Para, 9, Sao Paulo, Brazil; No. 65, Marjorie Stafford, University of Oklahoma Library, Norman, Okla.

(*Motion No. 12*) *Vote on applications for membership in the American Pharmaceutical Association.*

45. Applicant for Membership on Account of Contributions to the Headquarters Building Fund. The following non-member of the AMERICAN PHARMACEUTICAL ASSOCIATION has pledged $25.00 or more to the Headquarters Building Fund and has made a cash payment of $5.00 or more. He is entitled to membership and you are requested to vote on the application which has been properly endorsed.

No. H-3, Raymond B. Wissick, 8436 Michigan Ave., Detroit, Mich.

(*Motion No. 13*) *Vote on application of contributor to the Headquarters Building Fund for membership in the American Pharmaceutical Association.*

E. F. KELLY, *Secretary.*

WHO OWNS THE PRESCRIPTION?

The question of ownership of the prescription has been frequently discussed. A decision of the Supreme Court of Mississippi holds that—"Where the customer comes in to price a prescription the delivery to the druggist is conditional and limited. He is merely a custodian of it for the purpose of computing the costs, and he must immediately return it to the customer." The points of the case have been summarized that the title to the prescription: "Remains in the customer when it is submitted to be priced; resides in the customer until it has been delivered to the druggist for compounding; in the druggist after he has compounded the prescription and delivered the medicine to the customer; and reverts to the customer upon demand where the customer refuses to pay a price not previously agreed upon."

EVENTS OF 1932.

Quite a list of events of 1932 are embodied in the Historian's Report, November JOURNAL A. PH. A., beginning page 1220. Also in the reports of the Council, the General Sessions, the House of Delegates, the Sections, the Conference of Pharmaceutical Association Secretaries, Law Enforcement Officials—in the issues of the JOURNAL A. PH. A., beginning with the September number and in succeeding issues, including that of December.

Ground was broken July 1st for the Pharmacy Headquarters building.

On May 9th, Congress approved, by resolution, the use of the property owned by the AMERICAN PHARMACEUTICAL ASSOCIATION and such additional park property adjoining it as may be necessary to give the Building the location and setting required by these plans. The building is now under construction.

The Paris School of Pharmacy has completed a new building. The Pharmaceutical Society of Great Britain contemplates the erection of a new building. Massachusetts College of Pharmacy has added to its building.

The first distinct Library for History of Pharmacy was formally opened December 9, 1931, in Berlin. It is housed in the Institute for History of Medicine and Natural Sciences, part of the University.

The new Wellcome Research Institution, in London, houses various laboratories and museums, that contribute greatly to medical and pharmaceutical research.

Chairman E. N. Gathercoal prepared a history of the use of fluidextracts during the past fifty years. He is also collating prescription ingredient surveys.

Dr. Edward Kremers has in preparation phytochemical terminology; his contribution for 1932 includes a glossary of phytochemical terms with many references. He invites coöperation—see March JOURNAL, page 252.

Prof. John Uri Lloyd, with coöperation of Dr. Wolfgang Ostwald and Walter Haller, has published Physics in Pharmacy, part IV.

The Washington Bicentennial has renewed acquaintance with early American pharmacists, among them Charles Marshall, John Morgan, General Hugh Mercer.

"The Development of Pharmaceutical Education in the United States and Its Present Trend" contains historical data of early American pharmacy.

Leaflet No. 14—"Pharmacy," recently issued by the Department of the Interior, is one of a series of guidance leaflets designed for the use of high schools and college students, teachers, orientation classes, etc.

"Washington the National Capital"—Senate Document No. 332, 71st Congress, 3d Session, is a book of more than 700 pages, beautifully illustrated and bound. It has been prepared by H. P. Caemmerer, secretary of the Commission of Fine Arts. The AMERICAN PHARMACEUTICAL ASSOCIATION building graces page 497.

A new edition of the Chinese Pharmacopœia has appeared.

In commemoration of the 50th anniversary of its founding the Tokyo Imperial University is preparing a history of its fifty years' existence. The history of pharmacy will be included.

The 1932 Revision of the British Pharmacopœia has been issued.

The 5th edition of the Japanese Pharmacopœia has become official.

The Belgian Pharmacopœia has appeared and the Belgian National Formulary has been completed.

A conference of experts in vitamin investigations was held under the auspices of the U. S. P. Board of Trustees and Committee of Revision on May 7th.

One hundred years ago *Annalen der Pharmazie* had its origin, under the editorship of R. Brandes, Ph. L. Geiger and Justus von Liebig.

Das Chemische Zentralblatt, official publication of the German Chemical Society, celebrated its centennial year, January 1932.

The passing of the *Apotheker Zeitung* was announced in October by its editor, Hugo Kantrowitz.

The AMERICAN PHARMACEUTICAL ASSOCIATION held its 80th annual meeting in Toronto beginning August 22nd. The 25th annual meeting of Canadian Pharmaceutical Association was held during the same week and at the same place. Officials of the British Pharmaceutical

Society and Conference attended the meeting in Toronto—F. Gladstone Hines, president of the Society; H. N. Linstead, secretary; Herbert Skinner, chairman of the Conference, and Thomas Marns, member of its Council.

Henry S. Wellcome—prominent pharmacist, researcher, archæologist and head of many other undertakings—was knighted by King George.

Ottar Rygh, presented a report of his research work, resulting in the discovery of the formula and constitution of vitamin C, before the Norwegian Society of Science.

T. Potjewijd, pharmacist of the University Hospital, Leyden, has been elected Secretary-General of the International Pharmaceutical Federation.

Under direction of Chairman H. C. Christensen, of the Pharmacy Committee, the program for the pharmacy exhibit at the Chicago World's Fair is taking shape and will acquaint the public with the history and service of pharmacy.

The findings and data assembled by the National Drug Store Survey are being arranged for application by druggists.

"The Oersted" memorializes Hans Christian Oersted, Professor of Physics in the University of Copenhagen. He was the son of an apothecary and during his earlier years was employed in the pharmacy of his father. Hans Christian Anderson immortalized them in "The Two Sons of a Danish Apothecary."

The centenary of the discovery of chloroform was celebrated by scientific bodies throughout the world. Three scientists are entitled to consideration in connection with the discovery; namely, Samuel Guthrie, of the United States; Baron von Liebig, Germany; and Eugene Soubeiran, of France.

The Fourth International Congress on Medicinal Plants and Perfume-Yielding Substances was held in Paris during the week of July 16th.

The Liebig celebration was held at Giesen, Germany, July 19th, arranged for by the Society for Chemical Industry. Baron von Liebig in his early years was employed in a German pharmacy.

Dr. John J. Abel is the first pharmacologist to hold the office of president of American Association for the Advancement of Science, and the third representative of the medical sciences in the last thirty years, the other two being Dr. William H. Welch and Dr. Simon Flexner.

During March, biologists and medical men celebrated the fiftieth anniversary of the discovery by Robert Koch of the tubercle bacillus.

The 50th aniversary of the Red Cross was celebrated May 21st. Florence Nightingale was born May 12, 1820; Jean Henry Dunant, May 8, 1828.

Among the Golden Anniversary celebrants of the state pharmaceutical associations this year were the Maryland, Louisiana, Arkansas and Alabama associations.

Hon. T. G. Murphy, Canadian pharmacist, is member of the Dominion Cabinet; he is minister of the Interior and Superintendent General of Indian Affairs.

Professor Charles F. Heebner was elected *Honorary President* of the AMERICAN PHARMACEUTICAL ASSOCIATION.

The Remington Honor Medal was formally awarded to E. G. Eberle, October 12th.

The winner of the Fairchild Scholarship for 1932 is Julius Messina, of Baltimore.

Haussman Pharmacy, Philadelphia, won the 1931 National Pharmacy Week prize window display—the theme was, "Scientific Basis of the Prescription."

The limitation of world manufacture of narcotics and the control of drug distribution is undertaken by an international convention signed by the United States at the Geneva Conference on the Limitation of the Manufacture of Narcotic Drugs.

A copy of the report of the American delegation to this conference was made public by the Department of State, March 7th, in which the delegation urged ratification of the convention by the Senate.

Decision has been rendered in Chile that only pharmacists holding degrees from the University of Chile can practice pharmacy. Responsibility for enforcement of the law is vested in a "director general of public health."

The *National Pharmaceutical Syllabus*, 4th edition, has been published.

Final reports of the Committee on the Costs of Medical Care have been issued, a result of five years of intensive work and involving the expenditure of more than a million dollars.

The Council on Medical Education and Hospitals has adopted a resolution commending as one of the Essentials of a Registered Hospital that "the pharmacy of a hospital should be adequately supervised and should comply with State laws."

A uniform State Narcotic Law is being submitted to state legislatures for consideration; copies, with comments of drug and pharmaceutical organizations have, been mailed to all state and national associations for careful consideration before approval is given to the legislation.

A list of those who have ceased their labor is given in the November JOURNAL in the Historian's Report; others are listed here: W. A. Puckner, secretary of the Council on Pharmacy and Chemistry; Romaine Pierson, editor and publisher of *Practical Druggist;* Dr. John R. Minehart, dean Temple University, Pharmacy School; Dr. Gustavus Eliot, one of the founders of Connecticut Pharmacy School; John T. Moore, charter member of Kansas Pharmaceutical Association; David R. Millard, president Baltimore Veterans' Association; Frank Dubsky and William F. Baum, former presidents of Illinois Pharmaceutical Association; Bruno E. Knoefel, former president Indiana Pharmaceutical Association; Julius Greyer, former member of Ohio Board of Pharmacy; F. E. Holliday, former president Kansas Pharmaceutical Association and for many years associated with the National Wholesale Druggists' Association; Henry P. Thorn, former president of New Jersey Pharmaceutical Association.

TECHNOCRACY'S INADEQUACY.

The practices that have contributed most to depression and to every other economic evil have their foundations largely, if not wholly, in human traits, and the most malevolently potent of these are selfishness and greed. Unfairness in human relations is mankind's worst plague. Gold-standard currency is not the cause of unfairness. In the pioneer days of coonskin currency, all was not fair. There was Lincoln's early neighbor, for example, the "shrewd" backwoodsman who, when he came to the crossroads store to swap pelts for necessities, reminded the storekeeper's wife (she was alone in the store and could not find the proper weight for the "balances") that "a pint's a pound the world round." He was buying bullets!

The economic ills are ailments of mankind; not of machines; not of business. "The proper study of mankind" still "is man." The problem is only in small part technological.—From an editorial of *Oil, Paint and Drug Reporter*, January 16th.

TESTIMONIAL DINNER, HONORING PRESIDENT-ELECT ROBERT L. SWAIN AND SECOND VICE-PRESIDENT-ELECT JOHN C. KRANTZ, JR., A. PH. A.

Baltimore druggists are arranging a testimonial dinner for February 7th, at Hotel Emerson, honoring President-Elect Robert L. Swain and Second Vice-President-Elect John C. Krantz, Jr., of the AMERICAN PHARMACEUTICAL ASSOCIATION.

A committee has been named to arrange a program worthy of the occasion and under the direction of the Baltimore Branch, A. PH. A., all organizations of the pharmaceutical and drug-trade activities will join in the celebration. As is well known in association circles both of the honored guests are engaged in Public-Health work and active in a number of pharmaceutical, state and national organizations.

Doctor Swain received his degree in law from the Law School of the University of Maryland and Doctor Krantz is Professor of Pharmacology in the Medical School of the University.

William F. Reindollar, 2411 No. Charles Street, is secretary of the Baltimore Branch, A. PH. A.

WEST VIRGINIA NOT TO ISSUE ALCOHOLIC DRUG LICENSES.

Permits for druggists and other merchants to sell hair tonics, extracts and other liquids containing alcohol, except medicinal liquor, will not be issued for 1933, Tax Commissioner T. C. Townsend has announced.

Mr. Townsend, in a letter to Governor Conley stating his position, said that there is no official in the State who has the authority to issue such permits.

He said the statute requires the permits to be issued by the State Prohibition Commissioner, but as the Legislature last summer abolished the office and failed to designate another official to issue the permits, he would have no authority to issue them.

EDITORIAL NOTES

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PRODUCTION OF NARCOTICS.

According to the report of the Permanent Central Opium Board of the League of Nations on production of Morphine, Diacetyl Morphine and Cocaine in Germany, France, United States, Great Britain, Switzerland and Japan show large reductions in these countries, excepting the United States where there has been comparatively little change. Commissioner H. J. Anslinger commented on the report by saying that the decrease in European production has been due, in a large measure, to effective international coöperation in detecting origin of illicit traffic, and the distribution in the United States is held down, within legitimate channels, to a remarkable degree. Germany shows the largest reduction—the amount of morphine produced in 1929 was represented by 5031 Kg., in 1931, by 836 Kg.

SYRUP OF FERROUS CHLORIDE.

Gorton (*Svensky Farmaceutisk Tidskrift,* November 10, 1932), gives the following formula for this preparation, which has recently gained favor as a therapeutic agent for administering iron:

Iron, in powder	35	Gm.
Hydrochloric acid (17 per cent)	153.6	Gm.
Sugar	670	Gm.
Dilute hypophosphorous acid (10%)	10	Gm.
Distilled water	1000	cc.

Prepare in the same way as Syrup of Ferrous Iodide.—*Chem. & Drugg.*

ELIXIR EPHEDRINÆ HYDROCHLORIDI.

The pharmacopœial dose for ephedrine hydrochloride is from 1/4 to 1 1/2 grains, and the Committee on the British Pharmaceutical Codex is of the opinion that the maximum dose should be contained in each fluid drachm. There was also a suggestion that the presence of a proportion of alcohol minimized the persistence of the taste of ephedrine when exhibited in a glycerinated syrupy vehicle. The following formula is based upon one suggested by a member of the Committee, and is a stable and palatable elixir in which the taste of the ephedrine is well masked:

Ephedrine hydrochloride	Gm.	4.6
Distilled water	mils.	83.3
Glycerin	mils.	200.0
Glycerin of saffron	mils.	50.0
Spirit of chloroform	mils.	50.0
Alcohol (90 per cent)	mils.	125.0
Tincture of lemon	mils.	50.0
Syrup to make	mils.	1000.0

—*The Australasian Journal of Pharmacy.*

DANISH FORMULAS.

Emulsio Paraffini Liquidi DAK.—Paraffin Emulsion.

Tragacanth, in fine powder	5.0 Gm.
Solbrol	0.5 Gm.
Alcohol (90 per cent)	10.0 Gm.
Glycerin	150.0 Gm.
Distilled water	304.5 Gm.
Mucilage of acacia	30.0 Gm.
Liquid paraffin	500.0 Gm.

Dissolve the solbrol in the alcohol, add the tragacanth, glycerin and water. Set aside for a day or two, with occasional agitation. Then add the mucilage of acacia and the liquid paraffin and make an emulsion.—"Danish Formulary."—*Dansk Tidsskrift for Farmaci*, March 1932, page 64.

Liquor Barbipheni Compositus DAK.—Compound Solution of Phenylethylbarbituric Acid.

Phenylethylbarbituric acid	20 Gm.
Amylene hydrate	38 Gm.
Ethyl urethane	35 Gm.
Distilled water	7 Gm.

Maintain the mixture in a well-closed flask at a temperature of 20° to 30° C. until solution is effected; filter through a sterile bacteria-proof filter and sterilize.

Rectol DAK.—Chlorbutol Ointment.

Chlorbutol	30 Gm.
Calomel	30 Gm.
Liquid extract of hydrastis	12 Gm.
Extract of hamamelis	15 Gm.
Liquid paraffin	175 Gm.
White soft paraffin	200 Gm.
Wool fat paraffin	540 Gm.

Mix the chlorbutol with the calomel in a mortar and add the previously molten ointment basis when nearly cold. Then incorporate the extract of hamamelis and the liquid extract of hydrastis and fill in tubes provided with a rectal tube.

PERSONAL AND NEWS ITEMS.

Dean John Grover Beard, of the School of Pharmacy at the University of North Carolina, and Miss Gladys Angel, assistant professor of Physical Education at the University of North Carolina, were married at Liberty, N. Y., December 27th. The ceremony took place at the home of Judge and Mrs. Sidney F. Foster, the latter a sister of the bride.

Mrs. Beard is a graduate of Wellesley College and of Columbia University; the Dean is well and favorably known to pharmacists; he is the chairman of the Syllabus Committee, member of the faculty and dean of the School of Pharmacy, University of North Carolina. Best wishes are extended.

Mrs. John F. Hancock and Mrs. Charles E. Dohme, widows of former A. PH. A. presidents, passed the 92nd milestones of their lives this month. We hope for and wish them strength and health, but regret that at present they are not enjoying as good health as has attended them for many preceding years.

Former **President D. F. Jones** has favored the JOURNAL with clippings of the Watertown, S. Dak. papers commenting on the death and personal qualities of former President Coolidge. During the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in Rapid City, an elk barbecue was given by the hosts; the party stopped on the way to visit the temporary White House, and reminds us of the delightful visits with South Dakota citizens and pharmacists.

B. B. Brown, president of the Dallas County Druggists' Association, was reëlected to the office for the ensuing year. **Jerry McQuade** of *Drug Topics*, was one of the visitors at the annual meeting.

James F. Pickett has resigned the secretaryship of the United Medicine Manufacturers, after serving the organization for about twelve years.

Dr. Rodger Adams, of the University of Illinois, spoke on "Stereochemistry of Diphenyl," under the auspices of the Dohme Lectureship. Other speakers during the college year, under this lectureship, are Dr. Treat B. Johnson, of Yale University, and Dr. Irving Langmuir, of the General Electric Co. As is well known, this lectureship was founded in memory of Charles E. Dohme.

Dr. Paul H. Nystrom, professor of Marketing at Columbia University, speaking before the Mutual Buying Syndicate, Inc., New York City, said that "bargains have about played out and sales have been worked to death." He saw great need for a revision of selling practices, with one of the outstanding characteristics of present-day consumers being a "growing sensitiveness toward sales pressure. Customers won't stand for it. There is, however, ample opportunity for good salesmanship, salesmanship that finds the customers' viewpoint and serves the customers' requirements as fully and as helpfully as possible."

Botanists in various parts of the world are celebrating the centenary of the birth of the German botanist, Julius von Sachs, who founded plant physiology. A memorial program was carried out under the direction of Prof. D. H. Campbell, Stanford University, representing the Botanical Society of America; Prof. Rodney H. True, of the University of Pennsylvania,

representing the American Society of Plant Physiologists, and Prof. C. E. Allen, of the University of Wisconsin, representing the botanical section of the American Association for the Advancement of Science.

Representative Florence Kahn, of California, is one of the most outstanding champions in Congress for support of the American industries. She is appealing to women to buy their cosmetics from American manufacturers.

At a meeting of the Board of Governors of the Royal Commercial School for Orphans held in London, the Board accepted an offer of two thousand pounds a year from the trustees of the late Lord Leverhulme. One of the conditions of the gift is that the Board of Management shall undertake to direct those children who are orphans of chemists (pharmacists), to be nominated by the trustees.

Chairman E. J. Backus, of the Special Committee to Coöperate with Physicians and Dentists of the Illinois Pharmaceutical Association, has secured the publication of the code of Ethics of the A. PH. A. in Chapter 11 of the Chicago Medical Society. This Code of Ethics is likewise being distributed to pharmacy students.

The Oklahoma Board of Pharmacy has prepared a code of ethics which embodies the essence of the A. PH. A. Code. The following relates to service:

"To adopt the word Service, in its largest and fullest sense, as the watchword of my business, striving at all times to apply it to my dealings with my patrons, my competitor and my employees."

Dr. Charles L. Reese, retired chemical director of E. I. du Pont de Nemours and Company, Wilmington, Delaware, has been elected president of the American Chemical Society for 1934.

The Johns Hopkins University Institute of the History of Medicine commemorated on December 20th the three hundredth anniversary of the birth of Antony Van Leeuwenhoek, 1632–1723.

Samuel Shkolnik recently addressed the pupils of the Lake View High School on "Pharmacy as a Career." The talk was part of a series of addresses made under the auspices of the vocational adviser of the school.

At the recent meeting of the American Society of Tropical Medicine held in Birmingham, Alabama, on November 18th, Sir Henry S. Wellcome was elected an honorary member.

The Purdue School of Pharmacy has filled its one hundred thousandth prescription for the University Student Health Service. The Pharmacy School has been connected with this service since 1916 and its first prescription was filled by **Dean C. B. Jordan.** Nearly eighty prescriptions are filled daily, at this time. The prescription service is provided as part of the medical service.

SOCIETIES AND COLLEGES.

NEW YORK STATE PHARMACEUTICAL ASSOCIATION.

The officers and chairmen of the standing and special committees of the New York State Pharmaceutical Association, at a meeting held January 9, expressed themselves as not in full accord with the majority report of the Committee on Costs of Medical Care. A committee has been appointed by President Harry H. Miller, consisting of Dr. H. V. Arny, President Harry Goldschmidt, president of the New York Pharmaceutical Conference, Nicholas S. Gesoalde and Jacob Seley, to make a report at the annual meeting of the New York State Pharmaceutical Association to be held in Stamford, June 20th–23rd.

OHIO STATE PHARMACEUTICAL ASSOCIATION.

The Ohio State Pharmaceutical Association will hold its mid-year Convention at the Neil House in Columbus, January 25th–26th. The president is A. B. Ejbl; the secretary, Theodore D. Wetterstroem.

Business affairs and discussion of legislative matters will be the outstanding features of the meeting.

MINNESOTA PHARMACEUTICAL ASSOCIATION.

The Minnesota Pharmaceutical Association will hold its annual session at Lowry Hotel, February 7th to 9th. Round Table discussions will be a feature of the convention. The president of the Association is Harry Iverson and the secretary, Gustave Bachman. The Round Table Forum for Retail Druggists will be conducted by J. B. Christgau.

The Scientific and Practical Sections will be held on Wednesday, February 8th, and conducted by Dean Frederick J. Wulling.

A number of papers and addresses are

scheduled, and features of the meeting will be addresses by H. H. Gregg, Jr., and Dr. John O. Taft on "Unprofessional Relationships."

GEORGIA ASSOCIATION.

Georgia Pharmaceutical Association will convene in Augusta, May 23rd–24th, and celebrate its fifty-seventh birthday.

IOWA PHARMACEUTICAL ASSOCIATION.

Iowa Pharmaceutical Association will hold its annual meeting at Des Moines and also feature the drug show, February 14th to 17th. Among the speakers of the convention will be President John Goode of the N. A. R. D., Dr. E. F. Kelly, Secretary of the A. PH. A., and Dr. Robert L. Swain. Governor Herring has also been named among the speakers.

DEATH OF AL FALKENHAINER.

Al Falkenhainer, prominent in pharmacy for many years, died suddenly at his home in Algona, Iowa, December 20th. He was deeply interested in the Iowa Pharmaceutical Association, and saw the possibilities for pharmacy in the Northwestern Pharmaceutical Bureau and the Great Northwestern Drug Shows. He was actively interested in the insurance business of which he made a great success.

LEGAL AND LEGISLATIVE.

POISON LABELS.

While there is danger in medicinal substances, if used ill-advisedly, a poison label on every item that has caused injury is apt to do more harm than good. The accidents do impress that the sale of medicines should be restricted to those who are trained in pharmacy and, further, that grave responsibilities are assumed in the practice of pharmacy and of medicine. This is prompted by the suggestion made that Borax should be labeled as a poison. Every medicine and almost every food may, under certain conditions, do harm; these facts show the opportunity for sensationalists to create doubt in the minds of the public as to the value of medical and pharmaceutical service.

SALE OF DRUGS BY VENDING MACHINES CONTRARY TO LAW.

Chairman Robert L. Swain states that the matter of selling drugs by vending machines was taken up by the Conference of Pharmaceutical Law Enforcement Officials. This group called it to the attention of every board of pharmacy secretary, and urged that prompt action be taken in the several states to defeat any and all plans for the distribution of drugs through slot machines. Secretary M. N. Ford, of the Law Officials, reports that this effort of the Conference has received favorable comment, and that the matter will be dealt with promptly and effectively in the several states.

MEDICINAL SALES TO CUBAN HOSPITALS SEEM UNAFFECTED BY MEDICAL DISPUTE.

Distributors of medicinal preparations in Cuba have been following closely, for its possible effect on their sales, the dispute between members of the Medical Federation on the staffs of the various regional society hospitals and these regional societies. Members of these societies, such as te Centro Asturiano, Centro Gallego, etc., pay a monthly sum of $2 or $3, which entitles them to free medical attention, medicine and hospital care at the hospitals or quintas maintained by the societies. Doctors on the staffs of the "quintas" complain that many people who are financially able to pay current prices for their services are joining the societies where they get medical attention for a mere nominal fee, and the doctors in general are thus deprived of the opportunity to earn a living income.

RESTRICTIONS ON DRUG STORE SALES IN CUBA.

According to the *New York Journal of Commerce*—"An official Cuban decree recently issued stipulates that pharmacies may not have in their establishments other types of industry or commerce foreign to the profession, except drug supplies, scientific apparatus and stationery. They are also forbidden to carry in the same establishment articles other than those included in the foregoing list, even though they may be intended for free distribution. The application of this regulation, it is pointed out, not only prohibits the sale of candy, toys and other miscellaneous lines by drug stores in Cuba, but will now limit the giving of samples or premiums to strictly pharmaceutical items, toilet specialties or other similar articles. Cuban retail drug establishments, as a general rule, buy their stocks almost exclusively from wholesalers, rather than direct from the manufacturers. It has been the aim of the Govern-

ment to keep drug stores as far as possible on a professional rather than a commercial basis."

CONTERFEITING OF DRUG PRODUCTS.

Senator Copeland has introduced Senate Bill 5149 to prohibit counterfeiting of drugs. *Squibb's Message* states that "counterfeiting of nationally advertised medicinal and toilet products is rapidly increasing. Labels, containers, cartons and contents are being imitated to an extent never before known with a consequent menace to the public and the jeopardizing of the business interests of the respective manufacturers as well as of the retailers and wholesalers who may offer these counterfeit products for sale, unaware of their false character.

"In some instances, this counterfeiting has been so carefully carried out that the spurious nature of the product has been very difficult to detect. But the investigations have emphasized the existence of one avenue of safety for all dealers who would avoid such hazards; who would eliminate the dangers of confiscated merchandise and loss of business or professional prestige—it is that of buying only from reputable, responsible sources."

PURDUE BUSINESS CONFERENCE.

The third annual Purdue Druggists' Business Conference has been called for March 22nd and 23rd. This meeting is held each year under the direction of the Purdue University Pharmacy Extension Department; Indiana druggists have an opportunity to discuss their own problems among themselves. Approximately two hundred druggists have attended each of the conferences and were well pleased. During the last year's session a resolution was passed requesting the University to continue these meetings.

BOOK NOTICES AND REVIEWS.

Beginner Pharmacy. By HOMER C. WASHBURN, professor of Pharmacy and dean of the College of Pharmacy, University of Colorado, and CARL J. KLEMME, assistant professor of Pharmaceutical Chemistry, Purdue University School of Pharmacy. John Wiley & Sons, Inc., publishers. Price $2.75. Cloth, X, 231 + pages.

In the preparation of this book, as indicated by the title, the authors have not attempted to elaborate upon problems of advanced pharmacy, but the beginner is made acquainted with the subject-matter that is fundamental in the study of pharmacy. Topics are studied with a purpose to build up and create a desire for investigation.

In the Introductory, it might have been possible to refer to the "Guidance Leaflet" on Pharmacy, issued by the U. S. Department of the Interior, bringing the fact to the student's attention that he is entering upon studies which are to fit him for a public-health profession.

Part II is founded on Part I and deals with the "creative side of pharmacy"—the preparation of pharmaceuticals. The presentation of experiments has been well adapted for the discussions which accompany the experiments. Definitions for weighing, measuring, solution, extraction are given, but it seems to the reviewer that the "whys" could, perhaps, be more fully explained to the student, in a way that would stimulate a greater desire to study; in some instances there is too much briefness but, perhaps, in the authors' opinion this can be better left to the instructor. The problems contribute much to the explanations, for the selections have been thoughtfully made.

The Experiments of Part II add materially to the instructions, most of them answer the purpose but others are somewhat incomplete in that respect, for example—the tablets. It is, of course understood that the book deals with "beginner pharmacy," and that the knowledge and viewpoints gained are to serve the advanced study of pharmacy and its problems.

The authors are well and favorably known as teachers of their respective subjects and their work will serve a worth-while purpose. The mechanical part of the book is good, representative of the publishers.